BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 21 1951

# THE NEWER KNOWLEDGE OF ATHEROSCLEROSIS*

BY

J. B. FIRSTBROOK, M.D.

*(From the Banting and Best Department of Medical Research, University of Toronto, Toronto, Canada)*

In North America and northern Europe the degenerative arterial disease atherosclerosis has become a major cause of death—indeed, possibly the leading cause of death. There may be some consolation in the fact that the increasing death rate from this disease is partly a reflection of our increasing average life span, but far from reassuring is the high incidence of death and disability due to atherosclerosis among men in the prime of life. For this is not just a disease of old age. Coronary artery disease (about 95% of which is due to atherosclerosis) reaches its peak incidence as a cause of sudden death in men aged 50 to 55 (Rabson and Helpern, 1948), and, as is well known, death and disability from coronary disease in men below 50 are by no means rare.

An attempt will be made to sketch here the main outlines of our present knowledge of atherosclerosis, but several intriguing problems will have to be omitted or merely mentioned without elaboration.

## Terminology and Pathology

The term "arteriosclerosis" is unsatisfactory because it is used in various senses. To some it is synonymous with atherosclerosis; others use it to mean degenerative vascular disease in general. Occasionally, certain inflammatory arterial diseases are included under this heading. As the term arteriosclerosis has been applied to various diseases which differ pathologically and aetiologically, it is probably best, in the interests of clarity, to avoid it altogether and use a more specific terminology (Boyd, 1950).

*Medial sclerosis* involves mainly medium-sized arteries. Degeneration and calcification occur primarily in the medial coat of the vessel. Except as a rare cause of death in infants, this disease runs a benign and symptomless course.

*Arteriolar sclerosis* is a diffuse hyperplastic disease of the arterioles and is usually associated with hypertension.

*Atherosclerosis* affects mainly the large and small arteries. It predisposes to occlusion—particularly of the coronary, cerebral, and lower-limb vessels—and to haemorrhage, particularly from the cerebral vessels. The disease is characterized by a patchy and irregular deposition of lipids in the arterial intima, by intimal proliferation, and later by intimal and medial degeneration and calcification.

*An account of the original work discussed here was presented before the American Society for the Study of Arteriosclerosis, Chicago, Ill., November 5, 1950.

## Incidence and Mortality

How common is atherosclerosis? Unfortunately, during life the presence of the disease cannot be detected until lesions are well advanced and some clinical complication occurs. Even then the diagnosis of atherosclerosis is only presumptive. Palpable peripheral arteries indicate medial, not intimal, sclerosis. Calcification demonstrable by radiographs may indicate advanced atherosclerosis or only primary medial disease. The occurrence of myocardial infarction almost always indicates severe coronary atherosclerosis, but, because of the patchy and irregular distribution of the lesions, the full extent of the disease can be determined only at necropsy.

Fig. 1 shows the incidence of severe coronary atherosclerosis found in recent studies at the Mayo Clinic on the hearts of men and women who died between 30 and 90 years of age (Ackerman *et al.*, 1950; White *et al.*, 1950). The hearts of the men and women in each age group were examined consecutively regardless of the cause of death. The incidence in men reached a maximum in the 50 to 60 age group; but, beyond the age of 60, the percentage with severe lesions decreased, probably, of course, because the presence of severe coronary disease decreases the chances of survival to older ages. The incidence in women was lower than in men, but it tended to approach the male incidence beyond age 70.

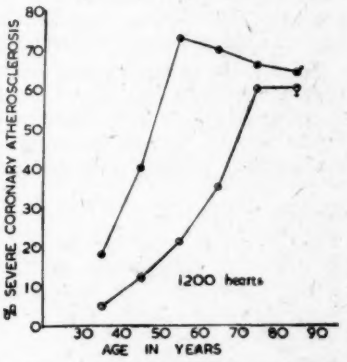



FIG. 1.—The incidence of severe coronary atherosclerosis at necropsy. Data of White *et al.* (1950) and Ackerman *et al.* (1950).

How important is atherosclerosis as a cause of death? This disease is not listed as a cause of death in official statistics, but from necropsy data one can estimate that about 95% of deaths from coronary disease (Wartman and Hellerstein, 1948), about 50% of deaths from cerebrovascular disease (Aring and Merritt, 1935), and about 50% of deaths assigned to diabetes mellitus (Millard and Root, 1948) are due to it. Atherosclerosis is a rare cause of death in men and women below age 25, but the mortality rises quite steeply with age and is not inconsiderable in men under 50.

### Aetiological Factors: (1) Time

What is the cause of atherosclerosis, and what factors influence its development? Although we have no definite answers to these questions there is a great deal of information available, and it is not accurate to state, as many have, that virtually nothing is known.

It is now generally agreed that atherosclerosis is not a natural or inevitable concomitant of ageing; it is a pathological process. It occurs in children with familial hypercholesterolaemia (Cook *et al.*, 1947) or with the hypercholesterolaemia associated with the nephrotic syndrome (Block *et al.*, 1948), and sudden death associated with severe coronary atherosclerosis, demonstrated at necropsy, has occurred in children as young as 11 years of age (Cook *et al.*, 1947). On the other hand, persons dying at advanced ages may have minimal or no atherosclerotic lesions (Allbutt, 1915). The incidence of the disease increases with age probably because the development of lesions is usually slow, and because hypercholesterolaemia (Keys *et al.*, 1950), obesity (Brozek and Keys, 1950) and hypertension (Robinson and Brucer, 1939) become more prominent with increasing age.

### (2) Hypercholesterolaemia

There are seven main lines of evidence suggesting that the plasma cholesterol is implicated in the development of atherosclerosis.

In the first place, the lesions have a high cholesterol content (Hirsch and Weinhouse, 1943).

Secondly, atherosclerosis has a high incidence and severity in a variety of diseases associated with prolonged hypercholesterolaemia: myxoedema (Bartels and Bell, 1939), diabetes mellitus (Millard and Root, 1948), the nephrotic syndrome (A. Steiner and Domanski, 1942), and familial hypercholesterolaemia (Bloom *et al.*, 1942).

Thirdly, the average concentration of cholesterol, particularly of esterified cholesterol, in the sera of men who have experienced myocardial infarction is significantly higher than in the sera of men in the same age group without clinical evidence of coronary disease (Gertler *et al.*, 1950).

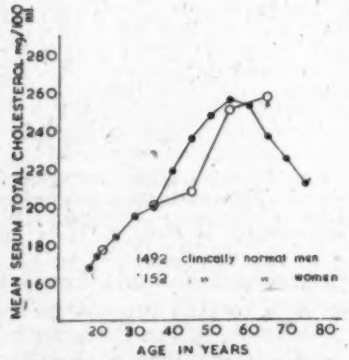



FIG. 2.—The relation between age and mean serum total cholesterol level. Data of Gram and Leverton (1949) and Keys *et al.* (1950).

Fourthly, as illustrated in Fig. 2, the average serum-cholesterol level of men increases with age and passes through a maximum at about 55 years. It will be remembered that this is approximately the age of maximum incidence of severe coronary atherosclerosis in males at necropsy and of the maximum relative incidence of coronary disease as a cause of death in males. Fig. 2 is based, in part, on the results of a recent investigation by Keys *et al.* (1950) in Minnesota. Reviewing the literature, they have found a similar trend in data from other parts of the United States and from Europe.

Gram and Leverton (1949) have reported that the average serum-cholesterol level of women increases with age. From their data and from the data of Keys *et al.* (1950), it would appear that the average levels are similar in men and women up to about age 40, but thereafter the average serum-cholesterol level in women is less than in men until about age 60. The highest average level was found in women 60 to 70 years of age—the oldest group examined by Gram and Leverton. The similarity of this trend to that of the incidence of coronary atherosclerosis in women is apparent, but the data for women are much less extensive than for men and must be interpreted with caution. The higher incidence of severe coronary atherosclerosis in men is unexplained. Dock (1950) believes that the greater depth of the coronary intima in males is a factor.

A fifth piece of evidence is that persons living on low-cholesterol diets, such as the Chinese, Okinawans, and Europeans subjected to food rationing, show, or did show, a low incidence of the disease (Sachs, 1949). Of course, this sort of evidence is only suggestive: dietary cholesterol is not the only variable factor involved.

P. E. Steiner (1946) examined 150 Okinawans, 18 days to 95 years of age, at necropsy; 40 were over 50 years old. Only one case of coronary sclerosis with calcification was seen; there were five cases of slight coronary sclerosis. No complications of vascular disease were seen in heart, brain, or kidneys. This low incidence of degenerative vascular disease is in striking contrast to American and European experience. Steiner reported that the diet of these people was largely vegetable in origin. Fat intake was low; meat and milk were taken infrequently. Their colons were large, long, and tortuous, similar to those of herbivorous animals.

The consumption of foods rich in cholesterol and the incidence of atherosclerotic complications both fell sharply in northern Europe during the 1939–45 war (Malmros, 1950; Strøm and Jensen, 1951). Data compiled by Malmros (1950) show a marked difference between the trends in the United States and Sweden. In Sweden the consumption of eggs and dairy products fell during the war; the consumption of eggs (the most important dietary source of cholesterol) and the death rate from "arteriosclerosis" (including diseases of the coronary arteries) both reached a minimum in 1942. In the United States, on the other hand, both the consumption of eggs and dairy products and the death rate from "arteriosclerosis" continued to increase throughout the war.

Obviously, there is no proof that the low cholesterol intake was responsible for these findings in Okinawa and Sweden. A low incidence of hypertension and especially of obesity probably played an important part.

A sixth line of evidence implicating cholesterol in atherosclerosis is the fact that typical atherosclerotic lesions have never been produced in animals without the administration of cholesterol either by mouth or by injection.

Cholesterol, a constituent of all animal cells, is synthesized in the body from relatively simple precursors (Bloch, 1950). In spite of this fact, there is no evidence that increased synthesis of cholesterol plays a part in the development of atherosclerosis in mammals. Birds differ from mammals in that the concentrations of the blood lipids, including cholesterol, are markedly elevated following the injection of oestrogens. Lipid-containing plaques may be produced in the arteries of chickens, even on a diet very low in cholesterol, if oestrogen is administered for several months (Chaikoff *et al.*, 1948; Horlick and Katz, 1948). However, these lesions differ from those produced in chickens by cholesterol feeding; they contain relatively little cholesterol in proportion to other lipids, and they exhibit relatively little intimal thickening (Chaikoff *et al.*, 1948). The lesions of so-called "spontaneous arteriosclerosis" seen in the coronary and other arteries of chickens maintained on a low-cholesterol diet contain very little cholesterol or other lipid; Paterson *et al.* (1948) believe that the coronary lesions result from primary medial disease.

Shortly after Windaus, in 1910, had demonstrated the high cholesterol content of human atherosclerotic lesions, Anitschkow showed that the disease could be produced in rabbits by cholesterol feeding. Anitschkow (1933) believed that the ingestion of cholesterol was the first and essential

event in the train of events leading to the development of lesions in animals and in man. Thus began a controversy which has continued for over thirty years. Leary (1949) and Dock (1950) have repeatedly defended Anitschkow's basic concept, but most authors have remained unconvinced.

In 1935 Duff discussed this subject in an excellent critical review which has had profound influence on subsequent work. He pointed out that the disease had been produced only in herbivorous animals, which normally eat a cholesterol-free diet, and that these animals develop a more marked hypercholesterolaemia than do omnivorous or carnivorous animals when fed cholesterol. He admitted that the experimental lesions are very similar to human lesions, but he stressed the fact that they are distributed differently. In 1942 Dauber and Katz produced atherosclerosis in an omnivorous animal—the chicken; and in 1946 A. Steiner and Kendall produced the disease by cholesterol feeding in a carnivore—the dog. The lesions in chickens and dogs are distributed very much as are human lesions. The disease has now been produced by cholesterol feeding in rabbits, guinea-pigs, chickens, dogs, and hamsters (Altschul, 1950), but it has never been seen in the rat (Horlick and Havel, 1948).

In the dog, it requires about a year of cholesterol feeding to produce gross lesions, but, if thiouracil is also given (with consequent depression of thyroid activity), hypercholesterolaemia is much more marked, and lesions develop in a few months. Thiouracil alone does not produce the disease (A. Steiner *et al.*, 1949). Similarly, in rabbits fed cholesterol, thyroidectomy increases hypercholesterolaemia and atherosclerosis, while thyroid administration inhibits both (Turner, 1933).

A seventh and final piece of evidence is that the severity of atherosclerosis in experimental animals is generally proportional to the degree and duration of the hypercholesterolaemia. Discrepancies do occur, but this does not necessarily mean that hypercholesterolaemia has nothing to do with atherosclerosis; it may only indicate the operation of other independent factors. One of these modifying factors is obesity or something associated with it.

### (3) Obesity

The high incidence of fatal atherosclerotic complications in the obese has been known to life insurance statisticians for a long time. Wilens (1947a, 1947b) concluded from a careful study of the findings in over 1,300 necropsies on men and women over 35 years of age that severe atherosclerosis is at least ten times as common in the obese as in the lean in each age group. Subjects of average adiposity had an intermediate incidence of severe lesions. Wilens (1947b) also found evidence that weight loss before death was associated with a resorption of lipid from the lesions in some subjects, but there was no good evidence that hyalinization or calcification was reversible.

This evidence that atherosclerosis is less severe in the lean suggested to us that variations in the degree of obesity, or some factor associated with obesity, might account in some part for the poor correlation often observed between blood-cholesterol level and severity of atherosclerosis. In order to examine this possibility, we have investigated the effect of food restriction on the development of atherosclerosis in rabbits.

#### Personal Observations

Some of the animals were allowed, throughout the experiment, all the Purina Rabbit Chow Checkers they would eat; others were restricted to 60, 50, or 40% of the food eaten by a freely fed animal of similar initial body weight. Each rabbit received daily by stomach-tube 1 g. of semi-purified cholesterol in aqueous suspension. Daily food consumptions and weekly body weights were recorded, and blood total cholesterol levels were determined weekly by the Schoenheimer–Sperry method. The animals were killed after four to seven weeks of cholesterol administration, and the sudan-stained aortae were graded as unknowns into five groups according to the area of intima involved by gross lesions.

The data obtained are summarized in the accompanying Table, with the animals arranged in order of increasing average blood-cholesterol level. Notice their wide variation, even among animals receiving cholesterol for the same length of time. There was no significant correlation between average blood-cholesterol level and weight change or initial weight. As might be expected, weight change was closely correlated with average food consumption. The initial weights of the animals were probably roughly proportional to their ages, but unfortunately their exact ages were unknown.

*Results of Experiment on Rabbits*

| Rabbit No. | Cholesterol Dosage (g. or Days) | Average Blood Total Cholesterol (mg./100ml.) | Initial Weight (kg.) | Weight Change (kg.) | Degree of Atherosclerosis | |
|---|---|---|---|---|---|---|
| | | | | | Found | Predicted |
| | $X_1$ | $X_2$ | $X_3$ | $X_4$ | Y | $\hat{Y}$ |
| 1 | 49 | 139 | 2·20 | +0·79 | 0 | −1 |
| 2 | 44 | 141 | 2·36 | +0·68 | 1 | 2 |
| 3 | 51 | 150 | 2·10 | +0·11 | 0 | 1 |
| 4 | 45 | 151 | 3·39 | −0·12 | 3 | 3 |
| 5 | 44 | 156 | 2·58 | −0·14 | 0 | 1 |
| 6 | 51 | 224 | 2·15 | +0·39 | 3 | 2 |
| 7 | 35 | 243 | 2·75 | −0·15 | 2 | 2 |
| 8 | 44 | 245 | 2·36 | −0·06 | 1 | 1 |
| 9 | 49 | 245 | 2·05 | +0·26 | 4 | 2 |
| 10 | 44 | 278 | 2·49 | +0·24 | 4 | 2 |
| 11 | 45 | 280 | 2·25 | +0·17 | 4 | 2 |
| 12 | 45 | 297 | 2·56 | +0·27 | 3 | 3 |
| 13 | 45 | 310 | 2·62 | −0·16 | 2 | 2 |
| 14 | 30 | 313 | 2·39 | −0·21 | 0 | 1 |
| 15 | 45 | 316 | 2·45 | +0·78 | 4 | 4 |
| 16 | 44 | 346 | 2·55 | +0·67 | 3 | 4 |
| 17 | 44 | 349 | 2·52 | −0·30 | 1 | 2 |
| 18 | 43 | 356 | 2·74 | −0·57 | 2 | 2 |
| 19 | 35 | 365 | 2·19 | −0·11 | 2 | 1 |
| 20 | 45 | 370 | 3·57 | −0·44 | 4 | 4 |
| 21 | 49 | 373 | 2·15 | −0·25 | 1 | 2 |
| 22 | 45 | 379 | 1·98 | +0·93 | 4 | 3 |
| 23 | 44 | 395 | 2·15 | +0·03 | 1 | 2 |
| 24 | 43 | 396 | 2·67 | −0·01 | 3 | 3 |
| 25 | 30 | 424 | 2·46 | −0·24 | 2 | 2 |
| 26 | 51 | 424 | 2·10 | +0·83 | 4 | 4 |
| 27 | 45 | 463 | 2·06 | +0·10 | 3 | 3 |
| 28 | 51 | 677 | 2·10 | +0·33 | 4 | 5 |

In a previously published account of this work (Firstbrook, 1950a), the weight changes were expressed as per kilogram of initial weight. Since, as Tanner (1949) has pointed out, the use of per-weight ratios may lead to spurious correlation, the weight changes are here expressed directly in kilograms and subsequent calculations have been made from these values. However, this change in the manner of expressing the results makes little difference to the correlations in this case.

Upon what does the degree of atherosclerosis depend? At first glance there seems to be no relation between atherosclerosis and the other variables. Actually, the degree of atherosclerosis is positively correlated with each of the other variables, but only in the case of average blood cholesterol is there a statistically significant correlation—that is, the chances that as high a correlation should arise from random variation alone are less than 1 in 20. However, on looking at the data, one is certainly not impressed by the relation between blood-cholesterol level and atherosclerosis.

It may be, though, that the severity of lesions is influenced by all four factors independently. If this is so, one would expect atherosclerosis to increase, in

general, with increasing blood-cholesterol level, but would expect modifications because of deviations in cholesterol dosage, in initial weight, and in weight change. For example, rabbit No. 4 had more atherosclerosis than animals of similar blood-cholesterol level; one notices that its initial weight was high—the second highest in the entire series, in fact. On the other hand, rabbit No. 25 had less atherosclerosis than might be expected; one notices that it lost considerable weight compared with animals with similar blood-cholesterol values.

The linear equation which best describes the relations between atherosclerosis and the other four variables can be calculated by the method of least squares. This equation is shown in Fig. 3. According to it the degree

| Estimated Atherosclerosis | | Dose | | Blood Cholesterol | | Initial Weight | | Weight Change |
|---|---|---|---|---|---|---|---|---|
| $\hat{Y}$ | $= -6.67 +$ | $0.043X_1$ | $+$ | $0.0069X_2$ | $+$ | $1.92X_3$ | $+$ | $1.85X_4$ |
| | | n.s. | | ** | | ** | | ** |
| | | 1 Degree | | 23 g. or days | | 144 mg./100 ml. | | 0.52 kg. 0.54 kg |

FIG. 3.—The linear equation of best fit for the data of the Table (n.s.=not statistically significant; **=statistically significant at the 1% level).

of atherosclerosis may increase, independently, with increasing duration of cholesterol feeding, with increasing average blood-cholesterol level, with increasing initial weight, and with increasing weight gain. The coefficients in the equation express the effect of each of the four independent variables on the degree of atherosclerosis. The coefficient for duration of cholesterol feeding is not statistically different from zero—that is, it may easily have arisen from random variation. This does not mean, of course, that increased duration of cholesterol feeding may not increase the severity of atherosclerosis; it means only that this experiment has failed to establish a significant relationship. This failure is probably due to insufficient spread in the total amounts of cholesterol administered. The other three coefficients are highly significant. The chances that they arise from random variation are, in each case, less than 1 in 100.

On the average, other things being equal, an increase in average blood-cholesterol level of about 144 mg. per 100 ml. is associated with a one-degree increase in atherosclerosis. Similarly, with other factors constant, an increase in initial weight of about 0.5 kg., or an increase in weight gain of about 0.5 kg., is also associated with a one-degree increase. It can be seen that, when all factors vary, the correlation between atherosclerosis and any one factor is likely to be poor. From a knowledge of dosage, blood cholesterol, initial weight, and weight change we can predict the degree of atherosclerosis quite accurately. Predicted values are entered in the last column of the table. There is a highly significant correlation between predicted and observed values; on the average, agreement as good as this would occur by chance alone less than once in 100 trials.

The rate at which aortic atherosclerosis develops in rabbits depends, then, not only on the degree of hypercholesterolaemia attained but also on the body weights of the animals at the beginning of cholesterol administration and on the amount of body weight gained or lost during the experiment. Other things being equal, the atherosclerotic process is inhibited in animals of relatively low initial weight, and it is inhibited in animals which lose weight or gain relatively little. This opens the way to control of the process.

### Inhibition of Experimental Atherosclerosis

Duff and McMillan (1949) and, independently, McGill and Holman (1949) have reported that the development of atherosclerosis in rabbits is inhibited by the induction of alloxan diabetes prior to cholesterol administration. A rapid loss of body weight is characteristic of severe uncontrolled diabetes in the rabbit. It is possible that the inhibition of atherosclerosis is largely associated with this loss of weight rather than with a more specific effect of the diabetes. An examination of the data of Duff and McMillan lends support, I believe, to this view. In animals receiving the same amount of cholesterol for the same length of time there is a general increase in atherosclerosis with increasing average serum-cholesterol level. An animal with less than the expected severity of lesions is found, in general, to have a low initial weight or a low or negative weight gain, or both. The diabetic animals tend to have lower initial weights than the controls, and they tend to show negative or small weight gains. Duff and Payne (1950) have recently reported that treatment with insulin partially removes the inhibition of atherosclerosis seen in diabetic rabbits. This is possibly due to the fact that insulin diminishes glycosuria and prevents or lessens loss in body weight.

Several groups of workers have reported that the administration of choline mixed with the food is associated with an inhibition of atherosclerosis in rabbits. It occurred to us that this inhibition might be due to appetite depression, with consequent depression of weight gained. In an experiment in which cholesterol-fed rabbits received 1 g. of choline chloride a day in gelatin capsules instead of mixed with the food, we found the degree of atherosclerosis to be closely proportional to the degree of hypercholesterolaemia; but we found no significant difference between choline-treated and control animals in average blood-cholesterol level or in weight change, and no evidence of an inhibition of atherosclerosis (Firstbrook, 1950b). Moses and Longabaugh (1950) have reported that, although the administration of choline with the food is associated with inhibition of atherosclerosis in rabbits, it is also associated with inhibition of weight gain.

## (4) "Unstable" Plasma Cholesterol

The fact that the degree of atherosclerosis is not always proportional to the degree and duration of hypercholesterolaemia has suggested to many workers that the physical state of the plasma cholesterol may be more important than its concentration.

All, or almost all, the cholesterol in plasma is bound to protein in large lipoprotein molecules. Gofman *et al.* (1950) have reported an analysis of these giant molecules in the ultracentrifuge. They have found in the sera of cholesterol-fed rabbits a type of lipoprotein molecule which is absent from the sera of normal rabbits, and the concentration of which approximately parallels the degree of atherosclerosis which develops. Similar molecules are found in many human sera. The percentage of men having detectable concentrations (5 mg. per 100 ml. or over) of these $S_f$ 10–20 molecules increases up to about age 60, and then declines somewhat—a trend similar to that shown by the average serum-cholesterol level; over age 40, about 50% of clinically normal persons harbour these molecules. Over 90% of myocardial infarction cases exhibit these particular lipoproteins, and their incidence and average concentration are increased not only in myocardial infarction but also in cases of coronary insufficiency, diabetes mellitus, hypothyroidism, familial hypercholesterolaemia, nephrotic syndrome, and hypertension.

The effect of a low-fat, low-cholesterol diet on them is of interest. Gofman *et al.* examined the effect of diets devoid of egg yolk and allowing only skimmed milk and 100–200 g. of lean meat daily as sources of animal fat. The diets contained less than 200 mg. of cholesterol a day—the average hen's egg contains about 300 mg. of cholesterol (Okey, 1945). When the diet was strictly followed, the concentration of $S_f$ 10–20 molecules fell in clinically normal persons and in persons with a variety of diseases. However, in common with serum-cholesterol levels (Wilkinson *et al.*, 1950; Keys, 1950), they showed no consistent relation to cholesterol intake among persons eating ordinary diets. Gofman *et al.* have found that some persons can tolerate large amounts of dietary cholesterol before these molecules appear in the serum, but, in others, the molecules decrease or disappear only when a low-cholesterol diet is strictly adhered to. Similarly, it would appear that drastic restriction of dietary cholesterol is necessary in many persons to effect a fall in the serum-cholesterol level (Keys, 1950).

It would seem to be a reasonable hypothesis that only the cholesterol present in plasma in a particular form, or forms, is involved in the pathogenesis of atherosclerosis, but it has not been satisfactorily demonstrated that the concentration of these special molecules is a more accurate measure of this "unstable" plasma cholesterol than is the total cholesterol concentration. Studies of free and esterified serum-cholesterol levels as extensive and carefully controlled as the ultracentrifuge studies of Gofman and his colleagues might produce equally striking results.

The relation of lipids other than cholesterol to hypercholesterolaemia and atherosclerosis is not clear. A high-fat diet may be expected to facilitate cholesterol absorption, but Keys (1950) has reported the aggravation of hypercholesterolaemia by feeding vegetable oil in a human subject on a diet free of cholesterol. Since the subject had familial hypercholesterolaemia, this finding may not be a general one. The administration of vegetable oil to rabbits does not produce hypercholesterolaemia or atherosclerosis, but further investigation in human subjects is desirable.

It has been suggested that a high ratio of serum phospholipid level to serum total cholesterol level is associated with inhibition of the development of atherosclerosis. This ratio is high in subjects with biliary obstruction, and, although there is marked hypercholesterolaemia, the incidence of severe atherosclerosis at necropsy is not increased (Ahrens, 1950). However, since phospholipid level is closely related to free cholesterol level (Popják, 1946), a high ratio of phospholipid to total cholesterol will occur whenever the free cholesterol is elevated to a greater extent than is the esterified cholesterol. In biliary obstruction there is a great increase in serum-free cholesterol and phospholipid concentrations, but a relatively small increase in esterified cholesterol. The low incidence of atherosclerosis in cases of biliary obstruction may be related to the low level of cholesterol esters rather than to the high phospholipid level. The fact that phospholipid plays a part in maintaining non-turbidity of serum may have no connexion with the genesis of atherosclerosis. Duff and McMillan (1949) found that inhibition of the development of atherosclerosis in diabetic rabbits was associated with increased, rather than decreased, serum turbidity.

The relation of lipid deposition to the production of degeneration in the arterial wall has long been a controversial question. Leary (1949) has presented evidence for his belief that crystalline esters of cholesterol cause a foreign-body reaction similar to that produced by silica in tissues.

### (5) Hypertension

Severe atherosclerosis is about twice as common in hypertensives as in non-hypertensives of the same age, sex, and adiposity (Wilens, 1947a). This is probably partly due to mechanical effects on the arterial wall, but the average serum total cholesterol (Watkin *et al.*, 1950) and $S_f$ 10–20 (Gofman *et al.*, 1950) levels are also higher in hypertensives. On the Kempner rice diet, which is free of cholesterol, the average serum-cholesterol level of hypertensives decreases to below the average level found in clinically normal persons on ordinary diets (Watkin *et al.*, 1950).

### (6) Arterial Damage

Mechanical or toxic damage to arteries predisposes to atherosclerosis at the site of injury (Duff, 1935), but there is no evidence that arterial damage is a prerequisite to lipid deposition.

## Conclusion

On the basis of present evidence, it would seem that the initiating cause of experimental atherosclerosis is the administration of cholesterol. However, because of the operation of modifying factors, not all animals receiving the same amount of cholesterol for the same length of time develop the same degree of lesions. In the first place, there is a wide variation in the degree of hypercholesterolaemia which develops. This variation depends probably on varying thyroid activity and possibly on other factors. In the second place, not all animals with the same degree of hypercholesterolaemia develop lesions at the same rate. Although, in general, the greater the degree of hypercholesterolaemia the more rapidly does atherosclerosis develop, variations in the degree of obesity, or some factor associated with obesity, can greatly modify the response. Finally, the rate of development of lesions is influenced by the arterial blood pressure and by pre-existing damage to the arterial wall.

What can be said about the aetiology and possible prevention of this disease in man?

So far as dietary cholesterol is concerned, although the *circumstantial* evidence is considerable, there is no *direct* evidence for the hypothesis that dietary cholesterol is involved in human atherosclerosis. Direct evidence for or against this hypothesis will be very difficult to obtain because of obvious difficulties in controlling a great diversity of factors, including diet, in a long-term investigation in human subjects. In the meantime, however, because of the high incidence of atherosclerosis as a cause of death and disability, it is important to consider whether dietary cholesterol should be restricted, and, if so, to what degree. It seems probable, in view of the experimental and clinical evidence, that it should be restricted, but the degree of restriction necessary to prevent the development of lesions will probably vary from person to person. Some persons, like some rabbits, can tolerate large amounts of dietary cholesterol before hypercholesterolaemia (or a detectable serum $S_f$ 10–20 level) develops, but others possess a low tolerance. In addition, of course, there is good evidence that the serum-cholesterol (or $S_f$ 10–20) level is not the only factor affecting the rate of development of lesions. Obviously, the question of restricting dietary cholesterol presents many difficulties.

Where myxoedema exists, its treatment would be expected to inhibit the progress of atherosclerosis; but desiccated thyroid must be administered very cautiously in the presence of coronary disease (Bartels and Bell, 1939). Conversely, the induction of hypothyroidism for the relief of angina pectoris would seem to be an unwise procedure because of probable acceleration of the underlying atherosclerotic process.

There is strong evidence from clinical, pathological, and experimental studies that an eminently desirable measure in the prevention of atherosclerosis is the prevention or correction of obesity. The virtues of a low-fat diet in this connexion are well known. A diet particularly low in *animal* fat has what may prove to be an additional virtue—a low-cholesterol content.

I am greatly indebted to Professor C. H. Best for helpful advice and criticism. The original work described in this paper has been made possible by a grant from the Canadian Life Insurance Officers Association.

REFERENCES

Ackerman, R. F., Dry, T. J., and Edwards, J. E. (1950). *Circulation*, **1**, 1345.
Ahrens, E. H. (1950). *Bull. N.Y. Acad. Med.*, **26**, 151.
Allbutt, C. (1915). *Diseases of the Arteries.* Macmillan, London.
Altschul, R. (1950). *Selected Studies on Arteriosclerosis.* Thomas, Springfield.
Anitschkow, N. (1933). In Cowdry's *Arteriosclerosis.* Macmillan, New York.
Aring, C. D., and Merritt, H. H. (1935). *Arch. intern. Med.*, **56**, 435.
Bartels, E. C., and Bell, G. (1939). *Trans. Amer. Ass. Stud. Goitre*, p. 5.
Bloch, K. (1950). *Circulation*, **1**, 214.
Block, W. M., Jackson, R. L., Stearns, G., and Butsch, M. P. (1948). *Pediatrics*, **1**, 733.
Bloom, D., Kaufman, S. R., and Stevens, R. A. (1942). *Arch. Derm. Syph., Chicago*, **45**, 1.
Boyd, W. (1950). *The Pathology of Internal Diseases*, 5th ed. Lea and Febiger, Philadelphia
Brozek, J., and Keys, A. (1950). *Science*, **112**, 788.
Chaikoff, I. L., Lindsay, S., Lorenz, F. W., and Entenman, C. (1948). *J. exp. Med.*, **88**, 373.
Cook, C. D., Smith, H. L., Giesen, C. W., and Berdez, G. L. (1947). *Amer. J. Dis. Child.*, **73**, 326.
Dauber, D. V., and Katz, L. N. (1942). *Arch. Path.*, **34**, 937.
Dock, W. (1950). *Bull. N.Y. Acad. Med.*, **26**, 182.
Duff, G. L. (1935). *Arch. Path.*, **20**, 81, 259.
—— and McMillan, G. C. (1949). *J. exp. Med.*, **89**, 611.
—— and Payne, T. P. B. (1950). Ibid., **92**, 299.
Firstbrook, J. B. (1950a). *Science*, **111**, 31.
—— (1950b). *Proc. Soc. exp. Biol., N.Y.*, **74**, 741.
Gertler, M. M., Garn, S. M., and Lerman, J. (1950). *Circulation*, **2**, 205.
Gofman, J. W., Jones, H. B., Lindgren, F. T., Lyon, T. P., Elliott, H. A., and Strisower, B. (1950). Ibid., **2**, 161.
Gram, M. R., and Leverton, R. M. (1949). *Fed. Proc.*, **8**, 384.
Hirsch, E. F., and Weinhouse, S. (1943). *Physiol. Rev.*, **23**, 185.
Horlick, L., and Havel, L. (1948). *J. Lab. clin. Med.*, **33**, 1029.
—— and Katz, L. N. (1948). Ibid., **33**, 733.
Keys, A. (1950). *Science*, **112**, 79.
—— Mickelsen, O., Miller, E. v. O., Hayes, E. R., and Todd, R. L. (1950). *J. clin. Invest.*, **29**, 1347.
Leary, T. (1949). *Arch. Path.*, **47**, 1.
McGill, H. C., and Holman, R. L. (1949). *Proc. Soc. exp. Biol., N.Y.*, **72**, 72.
Malmros, H. (1950). *Acta med. scand.*, Suppl. 246, p. 137.
Millard, E. B., and Root, H. F. (1948). *Amer. J. digest. Dis.*, **15**, 41.
Moses, C., and Longabaugh, G. M. (1950). *Arch. Path.*, **50**, 179.
Okey, R. (1945). *J. Amer. diet. Ass.*, **21**, 341.
Paterson, J. C., Slinger, S. J., and Gartley, K. M. (1948). *Arch. Path.*, **45**, 306.
Popják, G. (1946). *Biochem. J.*, **40**, 608.
Rabson, S. M., and Helpern, M. (1948). *Amer. Heart J.*, **35**, 635.
Robinson, S. C., and Brucer, M. (1939). *Arch. intern. Med.*, **64**, 409.
Sachs, B. A. (1949). *Amer. Practit., Phila.*, **3**, 284.
Steiner, A., and Domanski, B. (1942). *Amer. J. med. Sci.*, **204**, 79.
—— and Kendall, F. E. (1946). *Arch. Path.*, **42**, 433.
—— —— and Bevans, M. (1949). *Amer. Heart J.*, **38**, 34.
Steiner, P. E. (1946). *Arch. Path.*, **42**, 359.
Strøm, A., and Jensen, R. A. (1951). *Lancet*, **1**, 126.
Tanner, J. M. (1949). *J. appl. Physiol.*, **2**, 1.
Turner, K. B. (1933). *J. exp. Med.*, **58**, 115.
Wartman, W. B., and Hellerstein, H. K. (1948). *Ann. intern. Med.*, **28**, 41.
Watkin, D. M., Froeb, H. F., Hatch, F. T., and Gutman, A. B. (1950). *Amer. J. Med.*, **9**, 428.
White, N. K., Edwards, J. E., and Dry, T. J. (1950). *Circulation*, **1**, 645.
Wilens, S. L. (1947a). *Arch. intern. Med.*, **79**, 129.
—— (1947b). *Amer. J. Path.*, **23**, 793.
Wilkinson, C. F., Blecha, E., and Reimer, A. (1950). *Arch. intern. Med.*, **85**, 389.

# BACTERIAL FLORA AND BACTERIAL COUNTS OF INFANTS' BOTTLE FEEDS

BY

**JOYCE WRIGHT, D.M.**

*Member of the Medical Research Council's Scientific Staff*

*(From the Research Laboratories of the Hospital for Sick Children, Great Ormond Street, London)*

An account is given of the bacterial flora and bacterial counts of 300 infants' bottle feeds sampled in London during 1946–8. The feeds were obtained from children's hospitals, an infectious diseases hospital, residential nurseries, the out-patient department of a children's hospital, and an infant welfare clinic. Most of the samples were collected from the feeding-bottles immediately before the feeds were given; some, however, were obtained from bulk feeds prepared in milk kitchens. The feeds were of various composition and included reconstituted dried milk preparations, liquid cow's milk, expressed breast milk, thickened feeds, and clear fluids. The bacterial content may not have been representative of infants' feeds in general. Feed samples brought by mothers to out-patient and infant welfare clinics may have had their bacterial content increased during transport to them; on the other hand, in hospitals and nurseries, advice was often sought, and given, with regard to improved technique in feed preparation, and in two institutions at least this led to a reduction in the bacterial counts.

## Sources of the Feed Samples

*Children's and Infectious Diseases Hospitals.*—Hospital A (66 samples) and hospital B (22 samples) are children's hospitals. Most of the samples were collected in the wards and some in the central milk kitchens. In both hospitals, feeds sufficient for 24 hours were prepared, and were then stored in a refrigerator until required. Feeding-bottles in hospital A were autoclaved and in hospital B they were boiled; in both hospitals teats were boiled between each use. Hospital C (38 samples) is an infectious diseases hospital, and the samples were collected in the gastro-enteritis unit. Feeds were freshly prepared, as required, in the ward kitchen, except that certain thickened feeds were prepared in bulk, boiled, and stored either at room temperature or in the refrigerator for periods depending on the demand. Bottles and teats were boiled between each use.

*Residential Nurseries.*—Nursery X (22 samples) and nursery Y (32 samples) had central milk kitchens. Nursery Z (37 samples) had a milk kitchen on each infant floor, and practice regarding feed preparation varied in detail from floor to floor and from time to

time. Some feeds were prepared in jugs or feeding-bottles and stored in the refrigerator until required; others were freshly prepared for each feed. In all the nurseries bottles and teats were boiled between each use.

*Out-patient Departments.*—Bottle feeds, usually wrapped in a towel or napkin, were carried from home by some of the mothers bringing their babies to the out-patient department of hospital A (54 samples). As many of the mothers lived at a distance from the hospital, the interval between preparation of the feeds at home and sampling in the out-patient department was usually from one to three hours, occasionally as long as four hours. To the touch, the temperatures of the feeds varied from hot to cold; some mothers had had the feeds re-heated, at a restaurant or canteen or in the out-patient department, before the samples were taken.

*Infant Welfare Clinic.*—A few mothers attending the infant welfare clinic (29 samples) brought prepared bottle feeds with them, but the practice was not general. The interval between preparation of the feeds at home and the collection of the samples in the clinic was about half to one hour only, as most of the mothers lived within easy reach of the clinic.

### Composition of Feeds and Collection of Samples

Variations in the composition of the feeds, and their added sugars, minerals, and vitamins, were too numerous to allow of more than a broad grouping into the following classes: roller-dried cow's milk, half cream (97 samples) and full cream (84); spray-dried cow's milk (6); liquid cow's milk (13); expressed breast milk (11); thickened feeds—that is, with cereals, flour, etc., added—(35); special products—that is, lactic acid milk, citrated milk, casein hydrolysate, etc.—(18); clear fluids—that is, half-strength Hartmann's solution, saline, water, with or without glucose—(36). Particularly in the case of the hospital samples, milk feeds were often diluted, in varying proportions, with half-strength Hartmann's solution or with water; such diluted feeds have been classified according to their milk constituent.

In 260 of the 300 instances samples of the feeds were collected direct from the infants' feeding-bottles just before the feed was given. The feed therefore had already been warmed and the teat and valve placed in position before the sample was taken. The feed was shaken in the bottle, the teat removed, and a sample poured into a sterile screw-capped bottle. Forty samples were obtained from feeds prepared in bulk and stored in jugs or bottles. All the feeds examined were considered by the nurse or mother to be fit for infant consumption. When samples were collected at a distance from the laboratory they were refrigerated from the time of collection until the time of examination.

### Laboratory Methods

Feed samples, after removal from the refrigerator, were warmed to melt the fat and then shaken well.

*Bacterial Flora.*—A loopful of each feed sample was spread on a horse-blood nutrient-digest-agar plate, which was examined after two days' aerobic incubation at 37° C. In addition, from 235 of the 300 feeds a duplicate horse-blood nutrient-digest-agar plate was inoculated and examined after three days' anaerobic incubation at 37° C. Thirty-five of the samples were also cultivated on 7.5% NaCl nutrient-digest-agar for the isolation of staphylococci.

*Bacterial Count.*—Films of the feed samples were made on glass slides; those prepared from milk samples were fixed in methyl alcohol and stained with Newman's triple stain (Wilson, 1935), and those from clear fluids were fixed by heat and stained by Gram's method. The bacterial content was roughly estimated by microscopical examination on a grading from "very abundant" to "very scanty." Tenfold serial dilutions of each sample were made in quarter-strength Ringer's solution, the results of the microscopical examination serving as an indication of the range of the dilutions appropriate to each feed. Roll-tubes were prepared by the addition of 0.1 ml. of each dilution to each of three tubes containing melted "yeastrel" milk agar (Wilson, 1935). Colony counts of the roll-tubes were made after three days' aerobic incubation at 37° C. and the results expressed as the mean of the counts of the three tubes.

### Bacterial Flora of Feeds

The bacterial flora of the 300 infant feeds is listed in Table I. The results of the aerobic and anaerobic plates have been combined; in general, the flora of the two plates was the same, the exception being that the anaerobic plates showed a heavier growth of streptococci and a higher incidence of lactobacilli. The results of the bacteriological investigation of the milk feeds and of the clear fluids are shown separately.

TABLE I.—*Bacterial Flora of 300 Infants' Bottle Feeds*

| Bacterial Flora | Milk Feeds (264 Samples) | Clear Fluids (36 Samples) | Total (300 Samples) |
|---|---|---|---|
| *Micrococcus* | 142 | 11 | 153 |
| Aerobic spore-bearing bacillus | 99 | 2 | 101 |
| *Achromobacterium* | 66 | 4 | 70 |
| *Streptococcus* | 65 | 2 | 67 |
| *Bact. coli* | 15 | 11 | 26 |
| *Lactobacillus* | 25 | 1 | 26 |
| *Sarcina* | 23 | 1 | 24 |
| *Chromobacterium* | 8 | 0 | 8 |
| Yeasts | 2 | 5 | 7 |
| *Ps. pyocyanea* | 2 | 2 | 4 |
| *Staph. aureus* | 2 | 0 | 2 |
| *Neisseria* | 1 | 1 | 2 |
| *Proteus* | 1 | 0 | 1 |
| No growth | 38 | 18 | 56 |

*Milk Feeds.*—Table I shows that the predominating bacteria in the milk feeds were those commonly associated with milk and milk products—that is, micrococci, aerobic spore-bearing bacilli, achromobacteria, and streptococci. *Staph. aureus* (coagulase-positive) was found in only two of the 264 milk samples, and then in small numbers. Streptococci varied in their haemolytic activity on blood agar; many of them were alpha-haemolytic, some non-haemolytic, and a few beta-haemolytic. Only 13 of the strains were examined for Lancefield group; nine of these belonged to Group D and the remainder were not members of groups A, C, D, or G. *Bact. coli* was isolated from 15 (6%) of the 264 milk feeds examined; in 10 of these 15 feeds a heavy growth of the organisms was obtained. *Ps. pyocyanea* was found in two milk feeds and *Proteus* in one only.

*Clear Fluids.*—The term "clear fluids" was in certain instances a misnomer, for a number of these feeds were found on inspection to be cloudy with bacterial growth. Odours of fermentation products were emitted from some of the specimens. Yeasts were isolated in one hospital from five samples of half-strength Hartmann's-glucose oral fluid and from two milk feeds diluted with it. Dr. J. T. Duncan kindly examined 12 of these strains and was unable

to find that any of them belonged to a known pathogenic group—for example, *Cryptococcus* or *Candida*. He found several different species among the 12 cultures, and all appeared to be saprophytic types. *Bact. coli* was isolated from 11 (31%) of the 36 clear fluids; 10 of these 11 samples were half-strength Hartmann's fluid, with or without glucose, and the remaining specimen was regarded in the ward as sterile water. From 6 of the 11 samples a heavy growth of *Bact. coli* was obtained.

### Bacterial Counts of Feeds

The Chart shows the distribution among the 300 feeds of the colony counts in roll-tubes incubated at 37° C. for

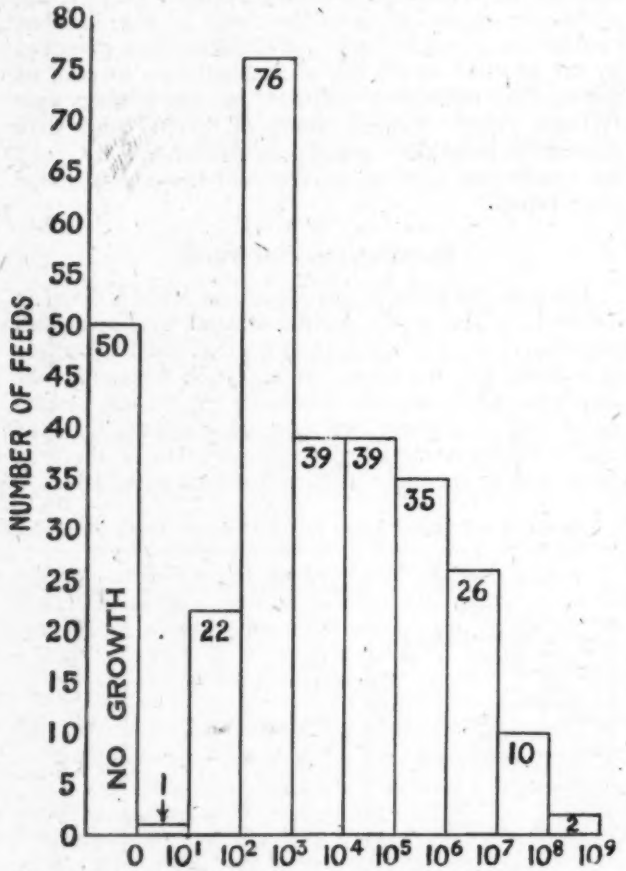



Chart showing distribution of colony counts per ml. of 300 infants' bottle feeds.

three days. Only 50 (17%) of the samples yielded a zero count—that is, no growth in dilution(s) counted. The distribution of the counts rose from 22 (7.3%) samples containing 10 to 100 colonies per ml. to 76 (25%) containing 100 to 1,000 colonies per ml.; it then fell gradually to reach a figure of 10 (3.3%) samples containing 10,000,000 to 100,000,000 colonies per ml. and 2 (0.7%) containing over 100,000,000 colonies per ml. The last two samples, one of diluted expressed breast milk and the other of cow's milk and groats, had colony counts of 880,000,000 and 136,000,000 per ml. respectively.

#### Colony Counts in Relation to Type of Feed

Table II shows the distribution of the colony counts of the 300 infants' bottle feeds in relation to their composition. As already stated, the constitution of the feeds within certain groups varied considerably, and this, together with the fact that the number of samples

TABLE II.—*Colony Count per ml. in Relation to Type of Feed*

| Type of Infant Feed | No. of Samples Examined | Colony Count per ml. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 0– | 10– | 10²– | 10³– | 10⁴– | 10⁵– | 10⁶– | 10⁷– | 10⁸–10⁹ |
| Reconstituted dried cow's milk | 187 | 23 | 1 | 18 | 49 | 24 | 27 | 26 | 15 | 4 | 0 |
| Liquid cow's milk | 13 | 3 | 0 | 1 | 3 | 2 | 2 | 2 | 0 | 0 | 0 |
| Expressed breast milk .. .. | 11 | 1 | 0 | 0 | 4 | 0 | 2 | 1 | 2 | 0 | 1 |
| Thickened feeds | 35 | 6 | 0 | 1 | 9 | 5 | 3 | 2 | 4 | 4 | 1 |
| Special products | 18 | 3 | 0 | 0 | 8 | 2 | 1 | 3 | 1 | 0 | 0 |
| Clear fluids .. | 36 | 14 | 0 | 2 | 3 | 6 | 4 | 1 | 4 | 2 | 0 |
| All types .. | 300 | 50 | 1 | 22 | 76 | 39 | 39 | 35 | 26 | 10 | 2 |

in each group was comparatively small, has rendered any attempt at statistical analysis impracticable. A few comments on the results may, however, be made. Among the 187 feeds of reconstituted dried cow's milk, only 23 (12%) gave colony counts of zero; 45 (24%) had colony counts exceeding 100,000 per ml., and 19 (10%) counts exceeding 1,000,000 per ml. One only of the 11 samples of expressed breast milk had a colony count of zero and 3 had counts exceeding 1,000,000 per ml.

Thirty-six samples of clear fluids were examined; only 14 (39%) had colony counts of zero, 7 (19%) had counts exceeding 100,000 per ml., and 6 (17%) counts exceeding 1,000,000 per ml. In several instances abundant bacteria were observed in stained films of clear fluids which, owing to terminal heat-treatment, yielded low counts of viable bacteria. Practice varied considerably regarding the treatment and storage of clear fluids. The type of container used for them included bottles with screw-caps, laboratory flasks with wool or gauze plugs, and discarded lemonade bottles with corks. Heat-treatment consisted of autoclaving, steaming, or boiling of the fluids and their containers. Storage was either in a refrigerator or at room temperature. Sterile fluids resulted where in-bottle autoclaving in screw-capped containers was the practice. Fluids with high colony counts of up to 20,000,000 per ml., and containing abundant *Bact. coli*, were found where storage had been at room temperature in corked bottles boiled (or in some cases washed only) at some uncertain date in the past.

#### Colony Count in Relation to Place of Sampling

TABLE III.—*Colony Count per ml. of Feed in Relation to Place of Sampling*

| Place of Sampling | No. of Samples Examined | Colony Count per ml. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 0 | 0– | 10– | 10²– | 10³– | 10⁴– | 10⁵– | 10⁶– | 10⁷– | 10⁸–10⁹ |
| Hospital A .. | 66 | 11 | 0 | 3 | 20 | 7 | 10 | 4 | 8 | 2 | 1 |
| ,, B .. | 22 | 7 | 1 | 6 | 5 | 3 | 0 | 0 | 0 | 0 | 0 |
| ,, C .. | 38 | 11 | 0 | 2 | 12 | 5 | 5 | 2 | 0 | 1 | 0 |
| Nursery X .. | 22 | 3 | 0 | 1 | 12 | 1 | 3 | 2 | 0 | 0 | 0 |
| ,, Y .. | 32 | 3 | 0 | 4 | 12 | 8 | 0 | 2 | 2 | 1 | 0 |
| ,, Z .. | 37 | 5 | 0 | 1 | 4 | 5 | 4 | 15 | 3 | 0 | 0 |
| Out-patient clinics | 54 | 7 | 0 | 0 | 5 | 6 | 12 | 8 | 10 | 5 | 1 |
| Infant welfare clinic .. .. | 29 | 3 | 0 | 5 | 6 | 4 | 5 | 2 | 3 | 1 | 0 |
| Total of feeds | 300 | 50 | 1 | 22 | 76 | 39 | 39 | 35 | 26 | 10 | 2 |

Table III shows an analysis of the colony counts of the infants' feeds according to the place of sampling. The incidence of feeds with colony counts of zero was low (9–17%) in all the places of sampling except hospitals B and C, which had figures of 32% and 29%

respectively. The reasons for the higher incidence of zero count feeds in hospital B, and also for the absence of counts exceeding 10,000 per ml., may have been that the number of babies catered for was comparatively small and therefore greater care in feed preparation could be exercised. A further reason may have been that the resident medical officer made the milk kitchen technique a matter of particular interest and responsibility.

In nursery Z, bottle feeds from the three infant floors were sampled at intervals over a period of 14 months. It was the practice in this nursery to prepare infant feeds during the night for use at 6 and 10 a.m. They were allowed to cool at room temperature and then stored in the refrigerator until required. Fourteen such feeds were sampled at 10 a.m.—that is, approximately six to eight hours after their preparation. The colony counts of these feeds ranged from 330 to 2,500,000 per ml. with a geometric mean of 40,900 per ml. The high count of certain feeds may have been due to bacterial growth occurring during the period of cooling and storage. The ready growth of organisms in milk feeds was shown by the fact that two feeds with initial colony counts of 500 and 200 per ml. had, after 24 hours' storage at room temperature, counts of 3,700,000 and 1,040,000 per ml. respectively. Storage would not account, however, for the original bacterial content of feeds; 11 milk feeds, sampled on two infant floors immediately after their preparation, had colony counts ranging from 7,700 to 414,000 per ml., with a geometric mean of 141,000 per ml.

It seemed possible that feeds were being prepared in imperfectly sterilized utensils, and jugs ready for use in one milk kitchen were examined bacteriologically. They yielded a heavy growth of micrococci, sarcinae, and achromobacteria. That bacteriologically satisfactory feeds could be prepared under the conditions provided was shown by the fact that the colony count of feeds was zero when the nurse-in-charge prepared them under the supervision of a bacteriologist. Three such feeds, even after storage for 16 hours in a refrigerator, had bacterial counts of only 0, 50, and 130 per ml.

The danger of storage of feeds was illustrated in other institutions also. In nursery Y milk feeds had been found to have colony counts of under 10,000 per ml. During a period of failure of the refrigerator the feeds were still stored in it though not chilled by it, and the counts of three feeds examined at this time were 2,050,000, 3,300,000 and 10,200,000 per ml. In hospital C the highest colony count—that is, 50,000,000 per ml.—was obtained from a thickened feed stored in the kitchen. The high counts which may result from storage of clear fluids have already been noted above.

Of the 54 infant feeds brought by mothers attending out-patient clinics with their babies, only 7 (13%) had colony counts of zero, 16 (30%) had counts of over 1,000,000, and 6 (11%) of over 10,000,000 per ml. Most of the feeds, as already stated, had been made up several hours before the samples were taken. Bacterial multiplication during this period of incubation would, however, seem unlikely to account entirely for such a high degree of contamination, which would more probably be explained by preparation of feeds in inadequately cleansed utensils in the home. One feed, for example, which had been made up only one-and-a-half hours previously, had a colony count of 69,000,000 per ml.

Repeated bacteriological examination of feeds of babies attending the out-patient clinics was not attempted owing to the distance of their homes from the hospital; it was not known, therefore, whether a high bacterial count was an isolated event or a constant feature of any particular baby's feed. Without this information one could not decide whether habitual ingestion of contaminated feeds had led to dietetic difficulties. Thirty-five of the 53 babies who had their feeds examined suffered from some form of digestive disturbance. Vomiting was a complaint in 15 cases, diarrhoea in 8, and both vomiting and diarrhoea in 6. The colony counts of the six feeds of this last group were: 1,870,000, 1,880,000, 8,340,000, 43,000,000, 46,000,000, and 69,000,000 per ml., and numerous *Bact. coli* were grown from four of them.

Colony counts of over 1,000,000 per ml. were found in the feeds of some babies with milder digestive disturbances and in a few instances from those of babies free from such symptoms. The evidence was not sufficient to incriminate contaminated feeds as a cause or contributory factor of digestive disturbance, but this matter would seem worth some further investigation. The milk feed of one habitual vomiter, for instance, yielded a colony count of 12,400,000 per ml. and contained abundant *Bact. coli* and Group D streptococci. Some 1,700 million of these organisms might be ingested, therefore, with each feed, and their fermentative and biochemical action on lactose and other feed constituents within the alimentary tract could conceivably result in gastric or intestinal disturbance.

Compared with the bottle feeds sampled in out-patient clinics, those brought by mothers attending an infant welfare clinic were, on the whole, of a bacteriologically cleaner quality. Even so, however, only 3 (10%) of these 29 feeds had a colony count of zero, and 4 (14%) of them yielded a count of over 1,000,000 per ml. The highest count among the feeds collected in the infant welfare clinic was 32,000,000 per ml.

### Observations on Feed Preparation Techniques

Certain errors and breaks in technique, all of which might lead to unsafe or unclean feeds, were observed during the present investigation: (*a*) absence of proper hand-washing facilities with elbow- or foot-operated taps; (*b*) failure to gown and mask while preparing feeds; (*c*) using a general ward kitchen for feed preparation; (*d*) cleansing of used bottles and teats in close proximity to the feed preparation table; (*e*) inadequate cleansing of bottles, teats, and utensils; (*f*) incomplete contact of bottle surfaces with boiling water in the sterilizer; (*g*) handling of teats with fingers; (*h*) drying of previously disinfected bottles with a glass-cloth; (*i*) returning used bottles, without prior disinfection, from the wards to the milk kitchen; (*j*) leaving warm bulk feeds at room temperature while awaiting distribution into individual feeding-bottles; (*k*) close packing of bottle feeds while still warm into the refrigerator; (*l*) storing of unsterilized feeds at room temperature; (*m*) exposure of bulk feeds, and of previously sterilized bottles and teats, to dust; (*n*) staff attending sick infants and also preparing feeds; and (*o*) lack of immediate attention to refrigerator breakdown.

The most important omission, however, was failure to place responsibility for feed preparation in the hands of one person trained in the principles of sterilization and milk hygiene.

## Discussion

The bacteriological results of the investigation indicate that infant feeds prepared in hospitals, residential nurseries, and private households may contain bacteria in large numbers. Only 50 (17%) of the 300 feeds yielded a colony count of zero; 73 (24%) had counts of over 100,000 per ml., and 38 (13%) of over 1,000,000 per ml. Recognized pathogens were rarely found, and *Bact. coli*, giving evidence of possible faecal contamination, was present in only 26 (8.7%) of the 300 feeds. Nevertheless, where high bacterial counts are found there is obviously a risk of contamination with pathogenic micro-organisms.

Bacteria may be introduced into a feed by the constituents of the feed, the bottles, the teats, or the utensils used in preparation. In the present study the bacteriology of the feeds was investigated immediately before ingestion by the infants, and no attempt was made to analyse the various factors which had contributed to their bacterial content. The organisms most often found were those commonly associated with milk and milk products—that is, micrococci, aerobic spore-bearing bacilli, achromobacteria, and streptococci. It seems unlikely, however, that bacteria in large numbers were introduced with the dried milk base of the feeds. Roller-dried milk powders taken direct from the plant were found (Higginbottom, 1944) to have a mean plate count below 1,000 per g. and rarely had a count in excess of 20,000 per g. Further, Dr. Constance Higginbottom (in a personal communication) reports that she examined, in 1943–4, 171 samples of roller-dried milk powders as supplied for infant feeding by food offices in different parts of Great Britain; the geometric mean count was 1,070 bacteria per g. with a range of 300 to 3,890 per g. In the case of thickened feeds and special products it was not practicable to assess the bacterial contribution of the various added materials. It is possible that heavy contamination of feeds was due to bacterial multiplication in the feeds before they were offered to the infant. In this connexion it may be noted that Higginbottom (1948) found that the mean plate count of reconstituted dried milk samples was increased 2,000-fold after storage for 24 hours at 22° C. Carriage of bacteria by unsterilized bottles, teats, or utensils may also be a source of contamination.

Other investigators (Lembcke, 1941; Lembcke, Quinlivan and Orchard, 1943; Rubenstein and Foley, 1947; Finley, Smith, and Louder, 1948; Rourke, 1947a; Cumming, 1949) have recorded bacterial contamination of supposedly sterile infant-feeding bottles, teats, and utensils used for feed preparation. Cumming (1949), for example, reported that drainage water from the teat container carried an average of 60,000 bacteria per ml. and that bottles after having been "washed and sterilized" each carried a load of about 80,000 bacteria. In an investigation on the collection of expressed breast milk in maternity hospitals it was found that contamination was mainly due to unboiled collecting-bowls and breast-pumps. The mean bacterial count of 2,230,000 per ml. of expressed breast milk was reduced by 99.3% when boiled collecting-vessels were used (Wright, 1947).

Unless close attention to detail is given at every stage of preparation, unsafe feeds carrying pathogenic bacteria and unclean feeds carrying large numbers of non-pathogenic bacteria may result. Rourke (1947a) found that feeds prepared even by the so-called aseptic technique had a "high incidence of bacterial growth." He considered that while it should be possible to prepare a sterile feed when personnel are properly trained, a good workroom is available, and equipment and materials are sterile, in actual practice these ideal conditions are rarely found.

### American Methods

Considerable interest has been shown in the United States of America in recent years in the problem of hospital milk-kitchen design and of procedures for the preparation of safe infant feeds. In general, there is agreement on the necessity for some form of terminal heat-treatment of feeds, and this process is being adopted by hospitals and health authorities throughout America. A survey of hospital milk-kitchen practice showed that details of the procedure varied considerably (Wallace, Abramson, and Losty, 1948). As a result of the bacteriological work of Rourke (1947a, 1947b), Smith, Finley, Wright, and Louder (1948), Finley, Smith, and Louder (1948), and other workers, methods recommended for terminal heating by the American Hospital Association (1949), and made obligatory by the New York State Health Department (1948a, 1948b) in hospitals and institutions caring for the newborn and in baby formula services, are as follows: (*a*) non-pressure heating requiring a temperature of 100° C. for 25–30 minutes either with flowing steam or with boiling water and steam in a water-bath, or (*b*) pressure heating with an exposure to 110° C. (6 lb. pressure) for 10 minutes.

Prior to heat-treatment the feeds are made up by a clean but not aseptic technique, placed in thoroughly cleaned but not necessarily sterilized bottles, and covered with teats and teat-caps; the whole feed unit is then submitted to terminal heating. The method has been shown to produce a high incidence of sterile feeds and teat surfaces. It eliminates pathogens but does not in all cases destroy heat-resistant spores. For this reason, immediate cooling of the feed units and storage in a refrigerator are required. The more drastic operation of exposure to 121° C. (15 lb. pressure) for 15 minutes, though producing sterile feeds, has been shown to cause physical and chemical damage to milk constituents; the two other methods described above, however, produced small losses only of the heat-labile substances, ascorbic acid, thiamin, and lysine (Hodson, 1949).

Scientific data and practical information regarding milk-room lay-out, equipment, and procedures are to be found in the manual by the American Hospital Association (1949), in a summary and review of this manual by Gillam (1949), and in two articles by Perkins (1949a, 1949b). For domestic use in private households, apparatus for terminal heating of bottle feeds by the non-pressure method has been put on the market and ordinary pressure cookers have also been used. In some American towns, sterilized infant feeds are prepared in and delivered by a central baby feed service.

### Need for Regular Bacteriological Inspection

Bottle feeds prepared for infant communities should be subject to regular bacteriological inspection in order to ensure that good techniques are constantly maintained. An acceptable standard for the bacterial count of the feeds is a problem for consideration. Cumming (1949) considered that bacterial counts of infant feeds, prepared by the aseptic technique but not subjected to

terminal heat-treatment, should, after 24 hours' storage, not exceed 500 per ml., and that no single count should be more than 10,000 per ml. He found that good procedure resulted in counts of less than 5 per ml. and that counts of over 100,000 per ml. pointed to errors in aseptic or mechanical procedures.

The New York State Department of Health requires that feeds, after terminal heating, shall be sterile upon bacteriological examination. This standard, though desirable, is likely to prove too stringent, as there is probably no method of terminal heating of feeds which can constantly ensure sterility without at the same time deleteriously affecting the chemical and physical properties of the milk. The American Hospital Association (1949) has therefore adopted a feed count of less than 25 organisms per ml. as an acceptable standard. Lowe (1947) used two standards for terminally heated feeds; (*a*) absence of coliform organisms, and (*b*) a maximum count of 50 bacterial colonies per ml. Rochester City (U.S.A.) Health Laboratory considered a maximum count of 100 colonies per ml. as satisfactory (see Lowe, 1947).

Maximum acceptable counts already suggested, therefore, are 500 colonies per ml. by Cumming for feeds prepared by an aseptic technique and 100 per ml. by the Rochester City Health Laboratory for terminally heated feeds. It may be noted that 162 (54%) of the 300 infants' bottle feeds examined in the present investigation yielded counts exceeding 500 per ml. and would therefore be unacceptable by the more lenient of these American standards.

### Model Milk Kitchens

A useful development in the public health field in this country might be the establishment at certain centres of model milk kitchens in which training of milk-kitchen supervisors could be undertaken. The investigation of improved and standard techniques suitable for infant units of various types and sizes could be a further object of their work. The safety measure of terminal heating is now well established in the United States. The method could with advantage be introduced for the sterilization of clear fluids used for prelacteal feeding and for oral administration to sick babies, but pilot studies would possibly be required to ascertain its applicability to the dried milk feeds in current use in this country. Improvement in feed-preparation procedures is also required in private households, and guidance might therefore be offered to infant welfare workers and health visitors at such special centres. While advance in milk hygiene and the introduction of legislation have promoted the supply of good quality liquid and dried milk to the general community, there still remains the problem of ensuring that it reaches the infant consumer in a safe and clean state.

## Summary

The bacterial flora and counts of 300 infants' bottle-feeds sampled in two children's hospitals, one infectious diseases hospital, three residential nurseries, one out-patient department, and one infant welfare clinic are recorded.

The composition of the feeds was as follows: roller-dried cow's milk, 181 samples; spray-dried cow's milk, 6; liquid cow's milk, 13; expressed breast milk, 11; thickened feeds, 35; special products, 18; and clear fluids, 36.

The bacteria most commonly isolated were as follows: micrococci and sarcinae, 177; aerobic spore-bearing bacilli, 101; achromobacteria and chromobacteria, 78; streptococci, 67. *Bact. coli* was isolated from 26 feeds, yeasts from 7, *Ps. pyocyanea* from 4, *Staph. aureus* (coagulase-positive) from 2, and *Proteus* from 1.

The distribution of the colony counts of the feeds in roll-tubes incubated for three days at 37° C. was as follows:

| No. per ml. | No. of Samples |
|---|---|
| 0 | 50 |
| 0– | 1 |
| 10– | 22 |
| 100– | 76 |
| 1,000– | 39 |
| 10,000– | 39 |
| 100,000– | 35 |
| 1,000,000– | 26 |
| 10,000,000– | 10 |
| 100,000,000–1,000,000,000 | 2 |

The range of the colony counts was from 0 to 880,000,000 per ml.

Among the 83 feeds prepared in private households and sampled in out-patient and infant welfare clinics only 10 (12%) had colony counts of zero, and 20 (24%) had colony counts in excess of 1,000,000 per ml. Possible association between high-count feeds and digestive disturbance is discussed.

Errors and breaks in the technique of infant-feed preparation in hospitals and nurseries were observed, and figures illustrating the result of preparing feeds in unsterilized utensils and of inadequate cooling and refrigeration of feeds are given.

The discussion deals with: the dangers of bacterial contamination of infant feeds by unsterilized bottles, teats, and utensils, and of bacterial multiplication during storage; a description of American methods of in-bottle terminal heat-treatment and a recommendation for their trial in this country; the need for regular bacteriological inspection of feeds prepared for infant communities; standards for bacterial counts of prepared infant feeds; consideration of the establishment of model milk kitchens for training supervisors, and for investigative work on improved procedures and equipment.

I wish to thank the Medical Committee of the Hospital for Sick Children, Great Ormond Street, London, for research facilities, and the medical officers, matrons, and nursing staffs of the hospitals, residential nurseries, and infant welfare clinic for their interest and help. I am particularly indebted to Dr. M. B. Alexander, Dr. R. E. Bonham Carter, Dr. E. H. Brown, Dr. D. H. Geffen, Dr. D. MacCarthy, Dr. A. P. Norman, and Dr. B. W. Powell.

### References

American Hospital Association (1949). Manual on Procedures and Layout for the Infant Formula Room.
Cumming, J. G. (1949). *J. Pediat.*, **34**, 711.
Finley, R. D., Smith, F. R., and Louder, E. A. (1948). *J. Amer. diet. Ass.*, **24**, 760.
Gillam, M. (1949). *Hospitals, Chicago*, **23**, No. 8, 41.
Higginbottom, C. (1944). *J. Dairy Res.*, **13**, 308.
—— (1948). Ibid., **15**, 285.
Hodson, A. Z. (1949). *J. Amer. diet. Ass.*, **25**, 119.
Lembcke, P. A. (1941). *Amer. J. Hyg.*, **33**, 42.
—— Quinlivan, J. J., and Orchard, N. G. (1943). *Amer. J. publ. Hlth*, **33**, 1263.
Lowe, R. H. (1947). *Mod. Hosp.*, **69**, 48.
New York State Dept. of Health (1948a). *Hlth News*, Supp., **25**, No. S.-7, February 16, 1948.
—— (1948b). Ibid., **25**, No. S-15, April 12, 1948.
Perkins, J. J. (1949a). "The Milk-Formula Laboratory." American Sterilizer Company, Erie, Pennsylvania.
—— (1949b). *Manual of Sterilization, Disinfection, and Related Surgical Techniques*, **10**, 3.
Rourke, A. J. J. (1947a). *Hospitals, Chicago*, **21**, No. 5, 67.
—— (1947b). Ibid., **21**, No. 6, 66.
Rubenstein, A. D., and Foley, G. E. (1947). *New Engl. J. Med.*, **236**, 87.
Smith, F. R., Finley, R. D., Wright, H. J., and Louder, E. A. (1948). *J. Amer. diet. Ass.*, **24**, 755.
Wallace, H. M., Abramson, H., and Losty, M. A. (1948). *Pediatrics*, **1**, 758.
Wilson, G. S. (1935). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 206.
Wright, J. (1947). *Lancet*, **2**, 121.

# RESULTS OF RE-EXAMINATION BY MASS RADIOGRAPHY

BY

**V. H. SPRINGETT, M.D.**

*Prophit Scholar of the Royal College of Physicians of London*

It is generally known that in England and Wales at the present time the maximum rate of mortality from tuberculosis occurs late in life for males, whilst in females the greatest mortality occurs in young adult life. There is little evidence of the source of these fatalities in later life in males : are they associated with a high attack rate of new disease in this period of life or are they due to breakdown of lesions acquired perhaps two or three decades previously ? This analysis of mass radiography results was undertaken in the hope that some evidence of relative attack rates at different periods of life might be obtained.

## Methods

During 1946 it was noticed that a considerable proportion (one-third) of persons attending a particular mass radiography unit in London had previously been examined by the same unit. It was a routine practice to note the fact of previous examination at the unit, so that it was possible, by having the record cards specially re-scrutinized, to obtain in age groups for each sex the numbers who had previously attended the unit. *X*-ray examination by other mass radiography units or elsewhere was not noted as a routine, so that individuals previously *x*-rayed elsewhere are included in the "not previously examined" group.

It was possible similarly to classify the patients with tuberculosis recalled for medical interview into those who had and those who had not been previously examined at the unit, and, by relating these figures to the numbers *x*-rayed, to obtain the incidence of tuberculosis in the two groups "previously examined" and "not previously examined." When a tuberculous lesion requiring investigation was found in a person who had been previously examined the recorded result of that previous examination was obtained and, if normal, the miniature film was re-scrutinized. Thus, these cases were further classified, either as radiologically new or as previously present. The mean interval between examinations was also estimated from the records : from this and the number of cases developing in a group of known size it is possible to calculate an "annual attack rate"—that is, the number of new cases occurring per annum per 1,000 at risk—in various age and sex groups. This annual attack rate is then compared with the annual mortality rate and with the incidence of disease found at first examination by mass radiography.

For my convenience the period of study was originally made to coincide with the period for which minimal lesions found by this unit were being recruited to the Prophit Survey (January, 1946, to April, 1948, for women ; January, 1946, to October, 1948, for men). Subsequently, further analysis was carried out so that the results of re-examinations of males in 1949 are included. The present paper deals not only with minimal lesions but with all tuberculous lesions found and considered to require clinical investigation after large-film reporting. All such cases have been reviewed and categorized either as "active" or "stable." For the purpose of this analysis "active" includes all cases showing, within an observation period of six months : (1) cavitation, (2) radiological progression, (3) isolation of tubercle bacilli, or (4) symptom-complex and/or signs of active disease : the presence of one or two commonly found symptoms such as cough did not lead to classification as "active."

Cases classified as "stable" either showed none of these features in a six-months observation period or, in a few cases, were classified as inactive on the result of the initial clinical examination. Although cases showing regression within six months are strictly active, for the present analysis they have been included in the stable group.

The mass radiography unit concerned is a static one examining Civil Servants in the London region. Most are clerical workers, though some are Post Office workers, and a few industrial Civil Servants are also examined. The exact percentage attending from any one office or group of offices is not known from unit records, but it is understood to be low, probably less than 50%. It follows that there has been no real clearing of possible sources of infection at places of work, as might occur at repeat examinations of a factory to which a unit went regularly and obtained a high percentage of attendances.

The procedures so far outlined can give no information concerning individuals who, after a normal examination, develop clinical tuberculosis and so are prevented from reattending. Very full records of all cases of tuberculosis in Civil Servants, leading to absence from work, have been kept since 1946 by the Treasury medical adviser's department. By the courtesy of that department it has been possible to have these records compared with the files of the mass radiography unit for the years 1943–9, and so to obtain information about cases developing symptomatically after a normal mass radiography examination.

## Results of Repeat Mass Radiography of Previously Normal Individuals

### Males

The results are shown in Table I. It is unfortunate that such comparatively small numbers were re-examined in the 15–24 year age group. The majority in this group were, in fact, over the age of 20. The reason for the small numbers is, of course, the absence of these young men on military service until well into 1946–7. On the small total available the incidence of new lesions of 4.7 per thousand in this age group is significantly greater than the incidence of 1.7 in the age group 45–59 years ; the difference between age groups 15–24 and 35–44 years is just not significant. The

TABLE I.—*Results of Re-examination by Mass Radiography of Males Previously Normal. January, 1946, to October, 1948, and January to December, 1949*

| Age (Years) | No. *X*-rayed | New Tub. Lesions | | Active Initially or Within 6 Months | Stable 6 Months |
|---|---|---|---|---|---|
| | | No. | No. per 1,000 | | |
| 15– | 2,531 | 12 | 4·7 | 7 | 5 |
| 25– | 9,325 | 26 | 2·8 | 16 | 10 |
| 35– | 8,119 | 17 | 2·1 | 4 | 13 |
| 45– | 10,575 | 18 | 1·7 | 10 | 8 |
| 60+ | 925 | 0 | 0 | 0 | 0 |
| Total | 31,475 | 73 | 2·3 | 37 | 36 |

incidence of 2.8 per thousand in the 25–34 year age group does not differ significantly from that in the younger age group nor from those in the older age groups : the steady decline in incidence with increasing age would seem a valid observation. The number of these cases giving evidence of activity or remaining stable for six months is also shown in Table I. There does not appear to be any constant relationship with age, and the cases are more or less equally divided between active and stable.

### Females

Table II gives corresponding results for females, though covering a shorter period of time. Adequate numbers have been examined in the younger age groups, but the totals are small in the older age groups. The age group 15–24 years includes a considerable proportion under the age of 20, so that this group is not comparable with the corresponding male group. There is, again, a sharp decline in incidence of newly appearing disease with increase of age, from 6.8 per 1,000 at age 15–24 years to about 1 per 1,000 at ages 35 and over.

TABLE II.—*Results of Re-examination by Mass Radiography of Females Previously Normal. January, 1946, to April, 1948*

| Age (Years) | No. X-rayed | New Tub. Lesions | | Active Initially or Within 6 Months | Stable 6 Months |
|---|---|---|---|---|---|
| | | No. | No. per 1,000 | | |
| 15– | 4,966 | 34 | 6·8 | 18 | 16 |
| 25– | 6,062 | 26 | 4·3 | 10 | 16 |
| 35– | 2,575 | 3 | 1·2 | 0 | 3 |
| 45– | 1,374 | 1 | 0·7 | 0 | 1 |
| 60+ | 36 | 0 | 0 | 0 | 0 |
| Total | 15,013 | 64 | 4·3 | 28 | 36 |

Only in the 15–24 year age group do the active cases outnumber the stable ones. Over the age of 34 years no new cases showing signs of activity in the six-months observation period developed in nearly 4,000 individuals examined.

### Annual Attack Rates

The interval between the mass radiography examinations varied greatly. In a few cases it was less than one year ; in a few it was as great as five years. For a sample of 850 women and 550 men attending for a repeat examination in 1946 or the first half of 1947 the interval from their previous examination was determined by re-scrutiny of both the relevant record cards. The age distribution of the sample agreed closely with the age distribution of the total, indicating that in this respect at least the sample was representative. The percentages of the sample reattending at various intervals are shown in Table III for men and women separately. The mean interval was 22.1 months for women and 19.1 months for men.

TABLE III.—*Percentage Distribution of Intervals Between Examinations*

| Interval (Months) | Female (%) | Male (%) |
|---|---|---|
| −15 | 41·0 | 35·5 |
| −21 | 25·5 | 35·5 |
| −27 | 10·5 | 12·5 |
| −33 | 11·0 | 8·0 |
| 34+ | 12·0 | 8·5 |

The difference in the means for men and women is not unexpected, as during 1943 to 1945 many of the younger men were in the Forces and were able to come to this unit for the first time only after completion of service. The inclusion of late 1947 and 1948 and 1949 cases in the sample would tend to increase this difference between the sexes, and for the whole material it is probable that the mean observation period is of the order of two years for women and one and a half years for men. If these figures are accepted as the best available approximation, and applied to those in Tables I and II, then annual attack rates of the order of 3.5 per 1,000 for women at age 15–24, 2 per 1,000 at age 25–34, and 0.5 per 1,000 over that age are obtained. Corresponding figures for men would be 3 per 1,000 at 15–24, 2 per 1,000 at 25–34, falling to 1 per 1,000 at 45–59. These rates must be regarded as low estimates, since cases developing symptomatically are not included.

## Cases Developing Clinical Pulmonary Tuberculosis after Normal Mass Radiography

When the records of the Treasury medical adviser's department were compared with those of the mass radiography unit, a further 29 cases were found which had developed clinically manifest tuberculosis after a normal mass radiography examination. It is, unfortunately, impossible to obtain attack rates from these cases, as there are too many unknown variables—individuals might not have reattended for mass radiography ; the population covered by the Treasury medical adviser's records is not exactly coextensive with the population examined by the *x*-ray unit. Some cases may have developed in individuals who left the Civil Service after a normal examination at the unit ; if so, there is no method of obtaining information about them, and to this extent there is a possibility of error in the following paragraphs.

However, the age and sex distribution of the 29 cases is of interest. In females 12 cases occurred at age 15–24, six at age 25–34, and none over that age. In males four cases occurred in the age group 25–34 years, three in each of the next two older age groups, and none over the age of 60. Only one case developed in the 15–24 year age group, but, as already noted, few young men of this age had been examined by the unit.

Although it is not possible to calculate attack rates from these cases the age distribution is essentially similar to that given by the mass radiography cases (Tables I and II). The annual attack rates derived from these tables are too low, but even from this small number of cases developing symptomatically it is most improbable that such cases would alter the age and sex relationship shown by the attack rates calculated from the mass radiography results.

The interval between the normal mass radiography examinations and the onset of clinically manifest disease in these cases is of interest, as it has been suggested by some that the onset of tuberculosis is usually sudden and hence that mass radiography is of little value. In females three cases developed within one year, nine in the course of the second year, three in the third year, and three after longer intervals. For males the figures were : one case in each of the first two years, five cases in the third year, and four after a longer interval. Again there are too many unknown factors to calculate attack rates for the various years, but, from the method of working, the numbers at risk in later years cannot be greater than in the first year and are likely to become less in each successive year. These results suggest that, while some cases do undoubtedly occur shortly after a

normal chest *x*-ray film, there is a period of lowered incidence of clinically manifest disease after mass radiography, extending over a period of one year for females and over the first two years for males. The difference between the sexes may be largely due to the fact that the males examined by the unit are on the average older than the females.

### Cases Showing Abnormality at Both Examinations

When re-scrutinizing the earlier miniature films of cases known subsequently to have developed tuberculosis a very strict standard was observed, as the main object was to obtain a valid attack rate of new lesions. Twenty miniature films were regarded as possibly showing lesions on which the original interpreter had made no comment—13 in women and 7 in men. All 13 women were under 35 years old, and fully half of them were reasonably passed as normal. The addition of a further six or seven cases as "new lesions" would still further increase the differences in attack rates between young adult and older females. The seven male cases with previous miniature films regarded as normal for the present analysis were more evenly distributed over the various age groups. Even if there were some newly developed cases included among these they could not seriously disturb the relationships between the calculated attack rates.

Of considerable clinical interest were the cases found to have active disease at the second examination which had definite lesions at the time of the earlier examination. In men, most of these cases were in the older age groups and had disease of a type which has usually been recognized as stable. Their importance is emphasized by the fact that there were 21 active cases in males aged 35 or over who had a lesion present at the previous examination, compared with 14 cases in this age group found to have active disease after a previously normal film.

Only two cases in women were assessed as "active" after having been previously regarded as stable. These patients were aged 30 and 34 years.

### Results of Initial Mass Radiography Examinations

*Males.*—Many mass radiography surveys have now been reported in the literature. The results given in Table IV are shown for comparison with those of Table I, as exactly the same standards of assessment have been employed. It should be noted, however, that the results in Table IV were collected during a shorter

TABLE IV.—*Incidence of Tuberculosis in Males First Examined by Mass Radiography. January, 1946, to October, 1948*

| Age (Years) | No. *X*-rayed | Active | | Stable | |
|---|---|---|---|---|---|
| | | No. | No. per 1,000 | No. | No. per 1,000 |
| 15– | 4,123 | 28 | 6·8 | 56 | 13·5 |
| 25– | 13,619 | 108 | 7·9 | 187 | 13·5 |
| 35– | 8,093 | 46 | 5·7 | 94 | 11·6 |
| 45– | 8,657 | 54 | 6·2 | 105 | 12·1 |
| 60+ | 1,091 | 8 | 7·3 | 17 | 15·6 |

period than those of Table I. There are no significant differences between age groups in the incidence of active or stable cases found on first attendance. The incidence of active cases in each age group is about 6 to 7 per 1,000. This is higher than the figure of 3 or 4 per 1,000 usually quoted, partly because the assessment is based on a six-months observation period and not a single clinical examination. The true incidence of stable cases is greater than that shown, especially in the older age groups: cases assessed as inactive on radiological appearances alone are not included, and these cases were probably more numerous in the earlier years of the study.

*Females.*—The results of initial examinations of females are shown in Table V for comparison with Table II. The incidence of active lesions is high—

TABLE V.—*Incidence of Tuberculosis in Females First Examined by Mass Radiography. January, 1946 to April, 1948*

| Age (Years) | No. *X*-rayed | Active | | Stable | |
|---|---|---|---|---|---|
| | | No. | No. per 1,000 | No. | No. per 1,000 |
| 15– | 9,339 | 72 | 7·7 | 91 | 9·7 |
| 25– | 6,992 | 51 | 7·3 | 117 | 16·9 |
| 35– | 3,537 | 16 | 4·5 | 57 | 16·1 |
| 45– | 2,391 | 4 | 1·7 | 27 | 11·3 |
| 60+ | 112 | 0 | 0 | 0 | 0 |

more than 7 per 1,000—up to age 35, but falls rapidly thereafter. The incidence of stable lesions remains fairly constant—just over 10 per 1,000.

### Annual Mortality Rates

For comparison with the annual attack rates the mean annual death rates per 1,000 for respiratory tuberculosis in England and Wales have been calculated for the years 1946–8 in the same age and sex groups that have been used throughout this paper. The rates are given in Table VI and show the familiar phenomenon of a rate

TABLE VI.—*Mean Annual Mortality from Respiratory Tuberculosis, England and Wales, 1946–8*

| Age (Years) | Males (per 1,000) | Females (per 1,000) |
|---|---|---|
| 15– | 0·36 | 0·67 |
| 25– | 0·62 | 0·70 |
| 35– | 0·67 | 0·39 |
| 45– | 1·06 | 0·25 |
| 60–64 | 1·18 | 0·25 |

high in young adult females falling to a low level in older life. The male rates start at a lower level than those for females, but rise to a high level in older life.

### Discussion

This statistical analysis indicates that the attack rate of radiologically detectable tuberculous lesions is similar in the two sexes—comparatively high in young adult life, falling with increasing age to appreciably lower levels in older males and to an almost negligible level in older females. A group of cases with symptomatic onset not included in the statistical analysis gives a similar age and sex frequency distribution, suggesting that the rates calculated may be too low in absolute value but supporting their general trend.

If these results are compared with the tuberculosis death rates in England and Wales during the period under review it is seen that there is a general similarity in the attack rates and death rates for females; both are high in young adult life and fall to low levels in older life. For males, however, the results are paradoxical: the highest attack rate occurs in young adults, but the maximum death rate occurs late in life, with the rate at 60 years nearly double that in young adults. It is suggested that a considerable proportion of these fatalities are the result of breakdown of lesions that

have been present for many years and probably acquired without major symptoms in young adult life 30 to 40 years ago. The results of the first mass radiography examinations reported here have shown, as in many other mass radiography surveys, that there is a considerable pool of inactive or doubtfully active cases amongst older males. The present study has further shown that breakdown of such lesions can and does occur, and is numerically as important in older males as newly acquired active disease.

While there is now an extensive literature covering mass radiography examinations, studies giving attack rates in age and sex groups of persons previously found normal are few in number. Dick and Thompson (1946) found very few cases developing even in household contacts over the age of 30; few cases would have been missed if contacts in this age group had not been repeatedly examined after one normal film. Dick (1948) has reported the results of repeat annual mass radiography examination of a factory group and showed a very low incidence of disease arising in those previously examined, the total of significant cases being of the order of 0.3% or 0.4%. The numbers involved were not large enough to permit of analysis by age and sex groups.

In the United States, Reid (1940, 1941) has reported the results of routine annual fluoroscopy of an office group: she gives the results for the years 1930–9 in broad age groups and shows an attack rate of 3 per 1,000 in young adults aged 17–29 of either sex, falling with increasing age to 1.4 per 1,000 at 40 plus for the first five years of her study and as low as 0.4 per 1,000 in the second five years. She shows little difference between corresponding age groups of the two sexes. She herself points out that some small lesions are likely to be missed on fluoroscopy, and of course re-scrutiny is not possible with this method.

Brooks (personal communication), in analysing the results of re-examination by mass radiography of men in the Royal Navy, found an increasing incidence of newly occurring disease with increase of age up to about 45 years. The older men in this study were mostly long-service men and constitute a rather special group with regard to environmental conditions. Cases occurring symptomatically are not included. Among women over 30–35 years in the W.R.N.S., Brooks found an extremely low incidence of newly appearing disease. In view of his results for older men, and the predominance of clerical workers in the present series, further studies along similar lines in other population groups would be valuable.

Following Frost (1939), I have shown elsewhere (Springett, 1950) on statistical grounds that the present peak of mortality in late adult life in males can be satisfactorily explained as the residue of even higher rates experienced by the group when young. The analysis in the present paper brings more direct evidence in favour of the view that the tuberculosis mortality of older males is to a considerable degree determined by the extent to which they as a group acquired disease as young adults, though the attack rate of new disease in older males cannot be regarded as negligible. For women also the mortality in later life is dependent mainly on the breakdown of lesions acquired in much younger life, and is only rarely due to disease acquired for the first time in middle life or later. The risk of breakdown is smaller than in males, however, so that there is in females at the present time no postponement of the age of maximum mortality, though there was such postponement at about the turn of the century.

## Conclusions

Certain practical conclusions follow from the results presented and the above discussion.

1. Mass radiography of a group not previously examined yields a greater incidence of active tuberculosis than similar examination of a group previously examined. This result is perhaps obvious, but it confirms that, until a community has been completely covered, the main effort should be concentrated on examining the greatest possible number of individuals for the first time.

2. At repeat mass radiography examinations the highest incidence of new lesions is found in young adults of both sexes. Few cases are found in older males and practically none in older females. When repeated examinations are possible the main effort should be to obtain the maximum attendance of young adults, as the chance of persons over the age of 35 years with a normal radiograph developing tuberculosis is so much smaller.

3. An essential corollary of conclusion 2 is that some arrangements must be made for further supervision of apparently healed or healing disease in older persons, particularly males, whether discovered by mass radiography or otherwise. Even annual radiological supervision in all such cases would seriously strain existing facilities in many districts. Special arrangements for their repeated examination by mass radiography is not satisfactory, as comparison of two 35-mm. films is difficult. Serial examinations require a method whereby films of one individual shall be filed together. If radiological supervision of apparently healed and healing lesions in older persons cannot be arranged, at least they and their private doctors should be informed of the finding, so that full investigation could follow immediately on the occurrence of symptoms. It must be admitted that such cases are commonly difficult ones to treat, but their detection and supervision are important from a public health aspect, and they should be advised on hygienic disposal of sputum.

## Summary

Repeat mass radiography of a group of males yielded 4.7 cases of tuberculosis per 1,000 examined at age 15–24 years, declining with increasing age to 1.7 per 1,000 at 45–59 years.

Similar examination of a group of females yielded 6.8 cases per 1,000 at 15–24 years, falling to below 1 per 1,000 at 45–59 years.

Expressed as annual attack rates the results were: Women, 3.5 per 1,000 at 15–24 years; 2 per 1,000 at 25–34; 0.5 per 1,000 over 34. Men, 3 per 1,000 at 15–24 years; 2 per 1,000 at 25–34; 1 per 1,000 at 45–59. These rates are low estimates, as no allowance is made in them for cases occurring symptomatically.

These results are compared with the incidence of tuberculosis found at a first examination by mass radiography and with the annual death rate from respiratory tuberculosis in England and Wales.

It is a pleasure to acknowledge the help received from many sources in compiling this paper. The medical staff of the Ministry of Health mass radiography unit has permitted ready access to all records, while the clerical staff has given help in the special analyses of record cards. Dr. Parks, of the Treasury

medical adviser's department, gave invaluable assistance on the section dealing with cases developing symptomatically. My contribution was part of the work as Prophit Scholar of the Royal College of Physicians, and the Prophit Committee of the College made additional clerical help available for the analysis of record cards.

BIBLIOGRAPHY

Dick, W. P. (1948). *British Medical Journal*, **1**, 689.
—— and Thompson, B. C. (1946). *Lancet*, **2**, 791.
Frost, W. H. (1939). *Amer. J. Hyg.*, **30**, 91.
Registrar-General. *Statistical Review of England and Wales*, 1946–7–8, Tables Medical. New Annual Series Nos. 26, 27, 28. H.M.S.O., London.
Reid, Ada C. (1940). *J. industr. Hyg.*, **22**, 303, 408.
—— (1941). Ibid., **23**, 35.
Springett, V. H. (1950). *J. Hyg., Camb.*, **48**, 361.

# TECHNIQUE OF JELLY (TUBERCULIN) SKIN-TESTING

## COMPARISON BETWEEN VARIOUS TECHNIQUES AND THE MANTOUX TEST

BY

**J. D. LENDRUM, V.R.D., M.B., Ch.B., D.P.H.**
*Chest Physician and Medical Director, Portsmouth Mass Radiography Unit*

It is apparent that many physicians reject the jelly test and that others are dissatisfied with results from this method. To a recent questionary sent to 246 chest clinics and children's and orthopaedic hospitals in England, 190 replies were received from different individuals (77%).

Of the 190, 80 (42%) do not use jelly tests, some having abandoned them. Of the 110 using the test, the number who abrade the skin with fine sandpaper was 64 (58%); in each group about one-third (35%, 36%) were dissatisfied with results. It is of interest to note that, of those who were dissatisfied, only 2.9% read their results at 72 hours or more.

The series of tests described was undertaken in order to find the most efficient method of jelly skin-testing, to produce a simple, standard, and reliable technique, and, if possible, to determine its equivalent in terms of the Mantoux test. The investigation was carried out independently of the work published by Pointon Dick (1950), and the draft article was written before his publication; some amendments in the text were made after the publication of his findings.

### Non-specific Reactions to the Mantoux Test

W.H.O. (1948) has lowered the final test dose of O.T. from 100 (1 mg.) to 10 tuberculin units (T.U.) on the grounds that there are non-specific reactions from the higher dose. It has been shown in America by Furcolow *et al.* (1941), Furcolow (personal communication), and Long and Seibert (1937) that such reactions occur with P.P.D. The former used increasing doses of P.P.D. and found that even infants under 6 months of age who had had no known contact would give a high proportion of positive reactions if the dosage was sufficient. They also stress the instability of the reaction, used by its opponents as a condemnation. Long and Seibert, using a timothy-grass (T.G.) product, found that 86% of those negative to first-strength P.P.D. and to the T.G. product in corresponding dosage, and who were positive to second-strength P.P.D., were also positive to the T.G. product in corresponding dosage.

The great advantage of the intradermal Mantoux test is claimed to be that an accurate known dosage is given. Furcolow and Robinson (1941) reported an interesting series in this connexion, injecting the same individual with the same material (P.P.D.) from the same syringe at the same time. With a dose of 1/10,000 mg. of P.P.D. they found that 3.3% were positive in one arm and negative in the other, and state that with higher dosage "much greater variation takes place"—a finding previously reported by Paretzky (1938). Heimbeck (1950) regards the Mantoux as not so good a test as the von Pirquet, mainly on the grounds of non-specificity.

*Standard for Comparison.*—The Mantoux test was regarded, for the purpose of this investigation, as the standard by which the various transdermal tests were measured, because it is still accepted in this country as the standard test, even at 100 T.U. dosage. It was felt that, if a test which was consistently equal to or better than 10 T.U. could be found, this would meet the objections to the use of the highest dose—objections considered by some to be exaggerated. The standard used for checking against false positive jelly reactions is therefore the 100 T.U. Mantoux test in those cases in which the 10 T.U. test gave a negative result and in which, therefore, a positive jelly test might be regarded as a false result; but from the work quoted above it appears to be more important to have a high correlation with the 10 T.U. test.

### The Techniques

Deane (1946) showed that abrasion of the skin by fine (grade O) cabinet-maker's sandpaper gave 100% positive results, using O.T. jelly, in a series of children known to be positive to the 1/1000 O.T. Mantoux test, whereas without the use of sandpaper only 87.5% were positive. The series was small and no details of age grouping were given.

*P.P.D. Jelly.—Technique A (P.P.D.):* The skin is given a firm rub with a plug of cotton-wool soaked in acetone; the interscapular area to be tested is then stroked lightly with flourpaper six times, so as not to produce an erythema; the jelly (60% w/v) is applied and covered with leucoplast. The plaster is removed at 48 hours, and the result is read 48 to 96 hours after application. The technique is that described by Pointon Dick (1950). *Technique B (P.P.D.):* Precisely as A (P.P.D.), except that, instead of a "firm rub" with acetone-wool, a deliberate attempt is made to produce an erythema with the wool, before flourpapering. *Technique C (P.P.D.):* This is a commonly used method in clinic practice. It is precisely as B (P.P.D.), except that the flourpapering is omitted.

*O.T. Jelly.—Technique D (O.T.):* Identical to A (P.P.D.), except that O.T. jelly replaces the P.P.D. jelly.

*Standards.*—In all tests in both parts of the investigation results were accepted as positive when the jelly gave six papules or more in the shape of the original application; and for intradermal tests an area of induration not less than 5 mm. in diameter. All O.T. was kept in a refrigerator when not in use and was discarded after 21 days from the date of dilution. All tests were performed and read by me.

### Results

*First Series. Technique A Compared with Technique C.*—Volunteers were 1,452 boys and 1,795 girls from schools in Portsmouth. The jelly tests were applied

to the interscapular area at the same time and were read between 48 and 96 hours later. The results are given in Table I. Thus 175 persons were positive and

TABLE I

| | | Results by Technique C | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Results by technique A | Positive | 175 | 243 | 418 |
| | Negative | 1 | 2,828 | 2,829 |
| Total | | 176 | 3,071 | 3,247 |

2,828 were negative to both tests; it is seen that technique A gave 243 positive results which were negative by technique C and missed only one which was positive to C. Of the 419 positive to one or other test, 418 (99.8%) were positive to A, but only 176 (42%) to C.

*Second Series. Technique B Compared with Technique C.*—Volunteers were 702 males and 498 females from schools and industrial concerns in Portsmouth. The results are given in Table II. Of those positive to

TABLE II

| | | Results by Technique C | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Results by technique B | Positive | 88 | 207 | 295 |
| | Negative | 0 | 905 | 905 |
| Total | | 88 | 1,112 | 1,200 |

one or other test 100% were positive to B but only 29.8% to C, 207 out of 295 positives being missed by technique C.

The results above suggest that technique B is an improvement over technique A, and a third series was undertaken to compare the two directly.

*Third Series. Technique B Compared with Technique A.*—Volunteers were 452 males and 502 females from a grammar school and two industrial firms in Portsmouth. The results are given in Table III. Of the 285

TABLE III

| | | Results by Technique A | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Results by technique B | Positive | 225 | 60 | 285 |
| | Negative | 0 | 669 | 669 |
| Total | | 225 | 729 | 954 |

positive reactions 100% were positive to B and only 225 (78.9%) to A. Of the 60 individuals showing a difference between the results, 57 were retested by Mantoux (100 T.U.) and each was positive.

*Sex and Age Groups.*—There is no significant difference in the results as between the sexes, and when divided into age groups the same trend is seen for all groups.

*Comment on First, Second, and Third Series.*—Table III shows that there is an advantage in the erythema factor, which is also used in technique C, but when technique C is compared with A (Table I), the advantage of flourpapering is seen to outweigh that of erythema. When techniques C and B are compared (here the *only* difference is the flourpapering) the advantages of flourpapering are even more clearly shown (Table II). It is possible that had results been read on the fifth or even the sixth day, instead of the third or fourth, more positive results would have been obtained with technique C, as entry of the tuberculin into the skin is presumably slower when abrasion is not used. The results show that of the P.P.D.-jelly techniques used B is the most sensitive, followed by A, with C the least sensitive.

*Fourth Series. Technique B Compared with Technique D.*—Volunteers were 417 infants and boys. The results are given in Table IV. Of the 20 differences

TABLE IV

| | | Results by Technique D | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Results by technique B | Positive | 134 | 0 | 134 |
| | Negative | 20 | 263 | 283 |
| Total | | 154 | 263 | 417 |

(D+, B−), 12 were positive by Mantoux 10 T.U., 7 by 100 T.U., and one was lost sight of. Results suggest that technique D gives results midway between 10 and 100 T.U. and is superior to the most sensitive P.P.D. technique.

## A Further Investigation

This investigation was undertaken in order to compare the efficiency of the O.T. jelly and the P.P.D. jelly, using the same—flourpaper—method, and to find their equivalent in terms of the Mantoux test in standard dilutions of O.T.

*Fifth Series.*—The jelly tests were applied to the interscapular area at the same time, and, as a result of experience gained in previous series, were read either on the fourth day or, more often, at the beginning of the fifth day. The Mantoux test was performed at the same time (approximately 20%) or on the day the jelly test was read; the Mantoux was read at 48 to 54 hours, with a small proportion, in the case of absentees (approximately 0.5%), at 70 to 74 hours. Volunteers were 867 males and 1,047 females, aged 4 to 20 inclusive, from schools and industrial concerns in Portsmouth. The results are given in Table V. This shows that the

TABLE V.—*Results by Technique D and Technique A*

| | | Result by D | | Result by A | | Total |
|---|---|---|---|---|---|---|
| | | Positive | Negative | Positive | Negative | |
| Results by 10 T.U. of O.T. | Positive | 712 | 1 | 632 | 81 | 713 |
| | Negative | 27 | 1,174 | 20 | 1,181 | 1,201 |
| Total | | 739 | 1,175 | 652 | 1,262 | 1,914 |

O.T. jelly failed to find only one case which was positive to 10 T.U., but the P.P.D. jelly (used by the same method) missed 81 such cases. The results of 10 T.U. Mantoux and technique D differed in 28 cases: in 27 the jelly was positive and the Mantoux negative—that is, the jelly was more sensitive—and in one the jelly was negative and the Mantoux positive. The results of 10 T.U. and technique A differed in 101 cases. In 20 the jelly was positive and the Mantoux negative, and in the remaining 81 the jelly was negative and the Mantoux positive. Compared with the Mantoux, the P.P.D. jelly test was somewhat unpredictable and in general less sensitive.

*Retest by Mantoux 100 T.U.*—The 1,201 individuals negative to 10 T.U. were retested by 100 T.U. Of the 27 positive to D, 24 were positive to 100 T.U. Similarly, of the 20 positive to A, 18 were positive to 100 T.U.

*Total Comparisons of Technique D and 10 T.U.*—Volunteers were of all age groups from 4 to 20 inclusive,

105 of these being infants. The results are given in Table VI. This shows that there were 49 differences in

TABLE VI.—*Total Tests by Technique D Against 10 T.U. of O.T.*

| | | Results by Technique D | | |
|---|---|---|---|---|
| | | Positive | Negative | Total |
| Results by 10 T.U. of O.T. | Positive | 1,213 | 1 | 1,214 |
| | Negative | 48 | 1,830 | 1,878 |
| Total | | 1,261 | 1,831 | 3,092 |

results between technique D and 10 T.U. of O.T., in all except one of these the Mantoux being negative: 39 of the 48 were tested by 100 T.U. and 36 gave positive results.

## Discussion

The low rates of positive reactions found in Portsmouth compared with other surveys (Price, 1948) call for the comment that 99.8% of all milk sold in the city is pasteurized.

*Efficiency of O.T. Jelly and P.P.D. Jelly in the Higher Age Groups.*—It has already been pointed out (fourth series) that technique B, the best technique with P.P.D. jelly, gave less good results than did technique D, with O.T. jelly; in the older age groups the P.P.D. jelly missed some 14% of the positives to O.T. jelly. In the fifth series 1,914 persons were tested by both O.T. and P.P.D. jelly, as well as by Mantoux; of these, 809 below the age of 14 showed a failure to O.T. jelly of 0.1%, and to P.P.D. jelly of 1.0%. Of the 1,105 persons aged 14 and over the O.T. failure rate was the same but the P.P.D. rate was 68%. The importance of this is that whereas transdermal tests have been considered to be unreliable in the higher age groups by those who regard this method of testing as a satisfactory one, including W.H.O. (1948), the failure in the higher age groups with technique D is no greater than the 0.1% of the under-14 age groups; this is not so for P.P.D. jelly.

*Efficiency of O.T. Jelly and P.P.D. Jelly Compared with 10 T.U. of O.T.*—The fifth series (Table VI) shows that of 3,092 individuals aged 4 to 20 the O.T. jelly test by technique D gave 3,043 results exactly comparable to 10 T.U. (98.4% agreement). Of the 49 discrepancies, 48 were positive jelly tests with a negative 10 T.U. test; of these 48, 39 were retested by 100 T.U. and 36 were positive. In 1,194 similar trials with P.P.D. jelly by technique A, 101 discrepancies were found, including 81 positives missed by the jelly test (Table IV). The results confirm the suggestion made earlier (fourth series) that the O.T. jelly test by this technique gives results which lie between 10 and 100 T.U. of O.T. and imply that the test is more sensitive than is suggested by Dick.

*Time of Reading.*—The impression was gained that the longer the interval, up to seven days, before the tests were read the more likely was it that a positive result would be given, especially with technique C. Experience gained in this investigation suggests that the fifth day is the optimum for reading jelly tests, but more work is being done on this aspect.

*Techniques Involving the Use of Erythema.*—In the first three series the techniques using erythema and flourpaper were shown to give the highest number of positive reactors; in the fourth series the technique using erythema and flourpaper with P.P.D. jelly was less efficient than flourpaper alone with O.T. jelly. Such combined techniques do cause trauma and may cause difficulty in reading results; Dick has stressed the need for controls until experience is gained, even with his technique, to guard against overuse of sandpaper. It is considered that the individual who develops an erythema when the skin is being cleaned is the one to be flourpapered very lightly.

*Severity of Reaction.*—The records in this investigation take no account of *degree* of reaction, although such results are probably more striking. In no case was complaint made of pain or disability with the jelly test, such as may occur with a severe Mantoux reaction; the worst complaint was irritation. It is suggested that the non-flourpaper technique, using either P.P.D. jelly (C) or, preferably, O.T. jelly, will pick out these hypersensitive individuals without severe reaction; technique D (O.T.) can then be used as the second test.

*Sensitizing Effects of Repeated Testing.*—It may be objected, in view of the fact that all persons had at least three tests and some five, that later results are open to doubt in view of a possible sensitizing effect from the first tests. It should be emphasized that, if a fact, this would tend to increase the number of positive intradermal tests, to the disadvantage of the jelly. Furcolow (personal communication) and Jones *et al.* (1949) state that there is evidence that there is no sensitizing effect; and Schwartzman *et al.* (1948) concluded that "studies which require repeated tuberculin tests are safe from the hazard of lasting sensitivity from these tests." Alston (1946), however, found that a previous intradermal test increased the number of positive reactors to the von Pirquet test. In any case the number of tests in any one individual in this series is small compared with those referred to.

*Relative Advantages of Transdermal and Intradermal Tests.*—Many tests have been devised. The Vollmer patch test was reported as being equivalent to 0.1 ml. of 1/1000 O.T. (10 T.U.), though 16% less sensitive to 100 T.U. (Hart, 1938; Quintos and Santiago, 1948). Alston (1946) disagrees, and Deane (1946) found only 80% positive with fresh material and 16% with patches 11 months old. Bell and Jerram (1945) condemned it, and most chest physicians have discarded it. The von Pirquet test, championed by Heimbeck (1950), is not so easy to use and is not regarded as adequate by Alston (1946) and Price (1948). The latter recommends the Dublin Moro test, followed by 100 T.U. of O.T. Alston (1946) finds that the Dublin Moro shows an 18% failure in relation to 100 T.U., but W.H.O. (1948) approves the use of the Moro test as the final test before B.C.G. in children up to 12 years of age.

It has already been pointed out that there are objections to the Mantoux test in high strength, of which the greatest is probably the non-specific reaction. If a test which has the accuracy of the Mantoux in lower strength, without its disadvantages of needing special apparatus and dry sterilization facilities, without the need for differing dilutions of short life (even with refrigeration facilities), with resulting unavoidable waste—if this can be found, it would be a test of immense value. The results reported here suggest that, properly used, the O.T. jelly is such a test material. Technique D has further advantages: it costs less than half as much in test material alone; the test material can be stored at room temperature and is easily portable; and, most important of all, this technique avoids the disruption of good relations between physician and child patients which may follow the Mantoux test. Many young adults also object to the test, and some refused to have a second injection, although negative to the first.

*Practical Use.*—It is considered that the jelly test might be of value as the final test prior to B.C.G. vaccination, in view of the evidence that its sensitivity lies between 10 and 100 T.U. and of the objections to the Mantoux test. A case has at least been made for its consideration and trial for this purpose. There would appear to be no doubt that for use in hospital, clinic, and general practice the test has many advantages over the intradermal test and has a failure of only 0.2% with O.T.; even this degree of failure must be considered in relation to the non-specific element of the intradermal test, referred to above.

**Summary**

Three techniques using P.P.D. jelly are described and are compared with each other in trials on some 5,400 persons of all ages from 4 to 20.

It is shown that techniques involving the use of flourpaper are essential if the best results are to be obtained. The use of the erythema factor alone gives poor and inconsistent results; its use in combination with flourpaper is not recommended as a deliberate policy.

There are some grounds for thinking that the less satisfactory results from the use of P.P.D. jelly are in part due to insufficient time being allowed before reading the test; the fifth day is suggested as the optimum for reading, but further work on this aspect is proceeding.

The use of O.T. jelly by technique D gives superior results to those of the same technique using P.P.D. jelly, and gave 98.4% agreement with 10 T.U. of O.T. in 3,092 cases aged 4 to 20, as opposed to 94.7% in 1,914 comparisons with P.P.D. jelly. The recommended technique is therefore technique D, which is that described and reported by Pointon Dick (1950).

Technique D (O.T. jelly) is as efficient in the higher age groups as in the lower, which is not the case with P.P.D. jelly.

The advantages of transdermal tests as opposed to the Mantoux test are emphasized; the jelly test has all the advantages of the former with none of the disadvantages of the latter, and when used as recommended is more reliable than 10 T.U. Its sensitivity level is between 10 and 100 T.U.—probably about half-way between the two.

It is to be preferred for hospital, clinic, and general practice to the Mantoux test; it is suggested that a case has been made out for its trial as the final test prior to B.C.G. inoculation, in view of non-specific reactions from 100 T.U.

I wish to express my thanks to Dr. J. Knowelden, of the Department of Medical Statistics, London School of Hygiene, for advice and assistance with the statistical part of the work; to the staff of the Chest Clinic and Mass Radiography Unit, whose willing help has made the investigation possible; and to the Medical Research Council for the provision of P.P.D. jelly and old tuberculin. Finally, I would like to thank the South-west Metropolitan Regional Hospital Board and the Education Committee of the Portsmouth City Council for the provision of a grant towards bus fares for children.

REFERENCES

Alston, Patricia (1946). *Irish J. med. Sci.*, **6S**, 130.
Bell, D., and Jerram, Ursula (1945). *British Medical Journal*, **2**, 215.
Deane, E. H. W. (1946). *Lancet*, **1**, 162.
Dick, W. Pointon (1950). *British Medical Journal*, **2**, 141.
Furcolow, M. L., Hewell, B., Nelson, W. E., and Palmer, C. E. (1941). *Publ. Hlth Rep., Wash.*, **56**, 1082.
—— and Robinson, E. L. (1941). Ibid., **56**, 2405.
Hart, F. D. (1938). *Lancet*, **2**, 609.
Heimbeck, J. (1950). *Tidsskr. norske Laegeforen.*, **70**, 1.
Jones, W. Wiley, Nelson, C., and Dwork, R. E. (1949). *Amer. Rev. Tuberc.*, **60**, 45.
Long, E. R., and Seibert, F. B. (1937). Ibid., **35**, 281.
Paretzky, M. (1938). Ibid., **38**, 81.
Price, Dorothy S. (1948). *Tuberculosis in Childhood*, pp. 22, 25. Wright, Bristol.
Quintos, F. N., and Santiago, C. (1948). *J. Philipp. med. Ass.*, **24**, 643.
Schwartzman, J., Schneider, M., and Crusius, M. E. (1948). *J. Pediat.*, **33**, 746.
W.H.O. Expert Committee on Tuberculosis (1948). WHO/TBC/3, 12. Geneva.

# POLIOMYELITIS IN ISLINGTON IN 1947, 1949, AND 1950

BY

**V. FREEMAN, M.R.C.S., D.P.H.**
*Medical Officer of Health, Borough of Islington*

In common with the county of London and also England and Wales, three substantial outbreaks of poliomyelitis were experienced in the Metropolitan Borough of Islington in each of the years 1947, 1949, and 1950. In all of these years the number of cases was considerably greater than had ever been previously experienced. However, as has been pointed out elsewhere, geographical distribution in poliomyelitis is very uneven, and each outbreak has its own peculiar and special features, as will be evident from the three outbreaks reported.

## Incidence and Mortality

TABLE I.—*Poliomyelitis and Polio-encephalitis Notifications and Deaths*

| Year | Population | Confirmed Cases | Rate per 1,000 of Population | Deaths | Case Mortality | Cases Under 5 |
|---|---|---|---|---|---|---|
| | | | *London* | | | |
| 1947 | 3,309,700 | 702 | 0·212 | 49 | 7·0% | 27·9% |
| 1949 | 3,389,850 | 668 | 0·208 | 50 | 7·4% | 55·3% |
| 1950 | 3,410,720 (Dec. 31, 49) | 456 | 0·133 | 35 | 7·7% | |
| | | | *Islington* | | | |
| 1947 | 236,840 | 22 | 0·093 | 4 | 18·0% | 27·3% |
| 1949 | 239,580 | 62 | 0·259 | 2 | 3·2% | 61·3% |
| 1950 | 240,370 (Dec. 31, 49) | 30 | 0·125 | 2 | 7·3% | 40·0% |

NOTE.—The deaths recorded are of cases included as confirmed cases.

Table I shows that in 1947 the Islington case rate per thousand population was considerably below that for London as a whole. The case mortality rate, at 18%, was two and a half times that for London. But the numbers are small and the difference may be due to chance.

The Islington case rates for 1949 and 1950 were comparable to those for the County of London, although mortality was low in 1949. The proportion of cases under the age of 5 varied considerably for each outbreak, the percentages showed reasonable approximations to the county figures for 1947 and 1949; the London figures for 1950 are not to hand.

With regard to the low case rate in Islington in 1947, Benjamin (1949) reported a significant negative correlation coefficient of −0.48 between the poliomyelitis attack rate and the average number of persons per room in each administrative area—that is, where more people were crowded together in the household there was less overt poliomyelitis. The extent of overcrowding did not materially alter in Islington in 1949 and 1950, but, as Breen and Benjamin (1950) mentioned in relation to the 1949 outbreak, immunity factors may well invalidate attempts to relate variations to social factors such as housing or economic environment.

## Epidemic Spread and Age Grouping

The attack in 1949 showed a sudden onset in July, without preliminary sporadic cases in Islington, and high peaks in September and October (Table II). 1950 gave earlier peaks in July and August with a gradual

TABLE II.—*Confirmed Cases of Poliomyelitis and Polio-encephalitis by Date of Onset*

| Year | Jan. | Feb. | Mar. | Apr. | May | June | July | Aug. | Sept. | Oct. | Nov. | Dec. | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1947 | | | 1 | 1 | | 1 | 2 | 6 | 4 | 4 | 3 | | 22 |
| 1949 | | | | | | | 9 | 6 | 17 | 18 | 8 | 4 | 62 |
| 1950 | 1 | | 1 | | 2 | 2 | 10 | 10 | 1 | 2 | 1 | | 30 |

increase from the earlier part of the year, and the slow rise to a maximum was also a feature in 1947. The difference in the under-5 distribution in each of the three outbreaks (Table III) has already been commented upon. Whether the 1949 age incidence is an exception to the general tendency for the age incidence to rise, as mentioned by Breen and Benjamin—a tendency which might appear to be confirmed by the 1950 age distribution—is a factor for future observation. In connexion with the high proportion of cases under 5 in 1949, and the more explosive character of the outbreak

TABLE III.—*Age Grouping of Cases*

| Year | Under 1 Year | –5 Years | –15 Years | –25 Years | Over 25 Years | Total |
|---|---|---|---|---|---|---|
| 1947 .. | 1 | 5 | 5 | 8 | 3 | 22 |
| 1949 .. | 3 | 35 | 17 | 2 | 5 | 62 |
| 1950 .. | 1 | 11 | 11 | 4 | 3 | 30 |

in this borough in July, it may be of interest to refer to the Eccles outbreak of 1947. Sweetnam (1949) noted there, in an outbreak with a somewhat similar sudden onset, that 60% of 46 total cases occurred in the 0–4 years group, as compared with only 31% in the country as a whole. This percentage is so close to that of Islington that it suggests the possibility of an age-grouping relationship to rate of spread.

## Poliomyelitis and Inoculations

Previous papers by Geffen (1950) and Bradford Hill and Knowelden (1950) have included information of Islington poliomyelitis cases in 1949 which may have been associated with recent inoculations. It may, however, be instructive to set out in more detail the differences in each of the three outbreaks for the respective years.

### 1947

In 1947 the total numbers were few, but, of six children under 5, only one suffered a left-arm paralysis. There was no case of "included" left-arm paralysis. ("Included" denotes that the site of inoculation was only one of the sites in which paralysis occurred.) This child was aged 19 months at the date of the onset of illness, and had had a second injection of 0.5 ml. of A.P.T. in the left arm five weeks before the onset. Considered alone, this case is of course of no significance, but it may have some significance in the light of the other reported cases.

### 1949

Table IV shows no undue incidence of left-arm paralysis in children over 5 who had had no recent inoculations or in those under 5 with no previous inoculations or with an interval of more than two months from inoculation to onset of poliomyelitis. The figures, however, are very different in those under 5 who were inoculated less than two months before the onset. Although not strictly comparable with the figures given by Bradford Hill and Knowelden, the proportion of left-arm sites of paralysis (46.8%) is considerably greater than in their cases.

TABLE IV.—*Sites of Paralysis and Previous Inoculation History in Children (Islington, 1949)*

| Site of Paralysis | All Cases up to 5 Years of Age | | | | Over 5 Years |
|---|---|---|---|---|---|
| | Interval Between Last Injection and Onset of Poliomyelitis | | No Previous Inoculations | Total | No Recent Inoculations |
| | Less than 2 Months | More than 2 Months | | | |
| Right arm .. | 2 | 1 | 3 | 6 | 1 |
| Left arm .. | 8 | 1 | | 9 | 1 |
| Right leg .. | 3 | 5 | 9 | 17 | 2 |
| Left leg .. | 2 | 8 | 9 | 19 | 3 |
| Trunk .. .. | 2 | 5 | | 7 | 2 |
| Cranial nerves.. | | 2 | | 2 | 1 |
| Polio-encephalitis | | 1 | 2 | 3 | 2 |
| Total .. | 17 | 23 | 23 | 63 | 12 |
| Cases with paralysis .. .. | 11 | 12 | 14 | | 10 |
| Cases with no paralysis .. | 1 | 2 | 2 | | 8 |
| No information | | | | | 2 |

This is emphasized in the detail of cases apparently associated with inoculations in Table V. Figures relating to other sites of paralysis did not appear to differ significantly from those usually obtained. It will be noted that 8 out of 20 of those over 5 years of age suffered no paralysis.

Table V deals in rather more detail with inoculated cases in which poliomyelitis developed shortly after inoculation. It will be seen that 11 of the 12 cases

TABLE V.—*Cases with Inoculation Histories up to Two Months Before Onset. 1949*

| Case No. | Age | Inoculations | | Paralysis |
|---|---|---|---|---|
| | | Type | Intervals | |
| 1 | 10/12 | Comb. A.P.T./pertussis | 13 days | Left upper arm |
| 2 | 18/12 | " " | 12 " | Left upper arm only. Deltoid group. Slight left-forearm weakness |
| 7 | 12/12 | A.P.T. | 5 weeks | Non-paralytic |
| 8 | 21/12 | Schick | 13 days | Left leg |
| 15 | 10/12 | Comb. A.P.T./pertussis | 14 " | Flaccid paralysis both arms, much more marked left side. Slight weakness of trunk muscles and diminution of movement at right hip |
| 16 | 15/12 | " " | 11 " | Left upper arm. Deltoid group |
| 22 | 23/12 | " " | 15 " | Whole left arm; finger movement slight |
| 24 | 27/12 | Pertussis | 17 " | Complete paralysis of upper and lower limbs and muscles of back |
| 28 | 14/12 | Comb. A.P.T./pertussis | 5 weeks | Left arm |
| | | A.P.T. | 9 days | |
| 30 | 18/12 | Pertussis | 6 weeks | No paralysis |
| | | Schick | 9 days | |
| 31 | 21/12 | Comb. A.P.T./pertussis | 6 weeks | Left arm, right leg (severe) |
| | | A.P.T. | 10 days | |
| 40 | 16/12 | " | 6 mths | Affecting right thigh, right, and left calves |
| | | Schick | 8 weeks | |

were aged 2 years and under, and that in fact all left-arm palsies except one (see Table IV) in those under 5 years were related to recent inoculations. The interval between inoculation and onset in the five children whose last inoculation was combined A.P.T./pertussis vaccine was 11 to 15 days; in one case there was a five-weeks interval following A.P.T. inoculation, with no paralysis; in one case a 13-days interval after a Schick test, with left-leg paralysis; in a further case a 17-days interval after pertussis vaccine, with extensive paralysis; an eight-weeks interval after a Schick test; and in the remaining three cases there had been two inoculations within the two months preceding the onset, with left-arm and "included" left-arm paralyses after final A.P.T. and initial combined injections.

It was important to ascertain the inoculating materials administered to all children, and Table VI shows the children dealt with at local health authority clinics in this borough during the period July 1 to September 26, 1949.

TABLE VI

| Type of Immunization | Year of Birth | | | | | | | Grand Total |
|---|---|---|---|---|---|---|---|---|
| | 1949 | 1948 | 1947 | Total | 1946 | 1945 | 1944 | |
| A.P.T. .. .. | | | | | | | | 91 |
| Pertussis vaccine only | 2 | 495 | 469 | 966 | 331 | 163 | 114 | 1,574 |
| Combined A.P.T./pertussis .. .. | 75 | 800 | 130 | 1,005 | 85 | 47 | 31 | 1,168 |

Of the 12 children with poliomyelitis after recent inoculations, eight were born in the year 1948, and the proportion of such children immunized with combined vaccine as against pertussis vaccine only was approximately 8 to 5, that with A.P.T. alone being almost negligible. Children who were given combined vaccine within two months of onset were therefore disproportionately attacked in the limb inoculated, whether alone or included. Inoculations with combined vaccine were suspended at the end of September, in view of the possible implications which then came to light on attention being drawn to them by Geffen (1950).

### 1950

In view of the previous year's findings, combined vaccine at clinics was not administered in the expected poliomyelitis season. Owing to the smaller number of children who contracted poliomyelitis in this year, Table VII is not broken down for age grouping in the same fashion as Table IV.

TABLE VII.—*Sites of Paralysis and Previous Inoculation History in Children of All Ages. 1950*

| Site of Paralysis | Interval Between Last Injection and Onset of Poliomyelitis | | No Previous Inoculations | Totals |
|---|---|---|---|---|
| | Less than 2 Months | More than 2 Months | | |
| Right arm .. .. | | 2 | 1 | 3 |
| Left arm .. .. .. | | 1 | 1 | 2 |
| Right leg .. .. .. | | 3 | 5 | 8 |
| Left leg .. .. .. | 2 | 2 | 7 | 11 |
| Trunk .. .. .. | 1 | 1 | 4 | 6 |
| Cranial nerves .. .. | 1 | | 4 | 5 |
| Polio-encephalitis .. | | | 1 | 1 |
| Total .. .. | 4 | 9 | 23 | 36 |
| Cases with paralysis .. | 4 | 4 | 12 | 20 |
| Cases with no paralysis .. | 1 | 4 | 3 | 10 |

TABLE VIII.—*Cases with Inoculation Histories up to Two Months Before Onset. 1950*

| Case No. | Age | Inoculations | | Paralysis |
|---|---|---|---|---|
| | | Type | Intervals | |
| 2 | 14/12 | Pertussis | 3 weeks | Left anterior tibial and left peroneal muscles |
| 14 | 5 years | ,, | 6 days | Back muscles |
| 15 | 3 9/12 | ,, | 2 months | Non-paralytic |
| 28 | 15/12 | A.P.T. | 2½ ,, | Left leg |
| 30 | 11/12 | ,, | 2 ,, | Right-sided facial palsy |

It will be noted that in 1950 there was no abnormal incidence of left-arm paralysis, and the distribution between upper and lower limbs conformed with the proportions customarily found. Thus 1950 would appear to emphasize the outstanding difference in inoculated limb paralysis which occurred in 1949.

Prophylactic inoculations in 1947, 1949, and 1950 have been administered in the main by the same two medical officers, and almost invariably the left upper arm is the part inoculated. The principal difference is that in 1949 up to the end of September, combined A.P.T. pertussis vaccine was the principal antigen used for children under 2 years. No abnormal incidence of local or general reactions to this antigen has been reported.

### Familial, Contact, and Group Cases

Breen and Benjamin (1950) reported that in the County of London more than one case in the same family was reported 14 times in 1949 and 27 times in 1947. They concluded that the numbers involved were so small that the results could not be regarded as statistically significant.

Bradley (1950) mentioned that multiple cases in a family or household are rare, but that this is not necessarily true on all occasions, and that before the end of 1950 there were already several instances. In the Isle of Wight, for example, there were three cases in each of three households, and this high infectivity was not accompanied by marked increase in virulence as expressed by mortality.

Gale (1948) investigated the possibility of cross-infection in hospitals and guardedly concluded that though cross-infection was rare it would be prudent not to admit into a general ward any patient who, by reason of a history of contact or of doubtful signs referable to the central nervous system, might be suspected of poliomyelitis. If a patient were admitted, then the discipline of typhoid nursing should be followed, particularly in the pre-paralytic and early paralytic stages.

So far as the Islington outbreaks are concerned, no familial or apparent contact cases were detected in 1947. Such cases, however, did occur in 1949, and to a greater degree in 1950.

#### Cases in 1949

*Case 17.*—Aged 3 years; onset, September 14; paralysis in lower limbs. *Case 18.*—Aged 16 months; onset, September 15; paralysis in lower limbs. These two children are brothers.

*Case 45.*—Aged 37 years; onset, August 24; non-paralytic case. There was no direct history of specific contact in this case, but the patient was an L.C.C. ambulance driver by occupation, and had recently transported poliomyelitis cases.

*Case 11.*—Aged 10 months; onset, July 23; paralysis in lower limbs. *Case 14.*—Aged 12 months; onset, July 17; paralysis in right upper arm group only. The degree of contact in these two babies, who lived near each other, is doubtful.

*Case 9.*—Aged 5 years; onset, July 20; meningismus; no residual paralysis. *Case 10.*—Aged 3 years 9 months; onset, July 23; polio-encephalitis. These two children are brothers.

*Case 50.*—Aged 7 years; onset, about September 15; palatal paralysis. *Case 34.*—Aged 3 years 8 months; onset, October 25. Left lower limb paralysis. So far as was known there was no contact between these two children, who lived near each other.

*Case 5.*—Aged 3 years 5 months; onset, August 31; paralysis in lower limbs. *Case 54.*—Aged 6 years; onset, October 31; paralysis in left shoulder. There was no known contact between these two children, who lived near each other.

In connexion with Case 5, it was ascertained that his brother, aged 9, vomited on August 31 and complained of pains in the legs; he was drowsy on September 4, and was seen by his own doctor, who was not informed of the illness

and prior removal of Case 5 to hospital. No further action was taken in respect of the brother, who apparently recovered rapidly and completely.

It could therefore be said from the above cases that there was familial incidence in two families, and possibly in three families, with an abortive or minor case in the third.

#### Cases in 1950

*Case 28.*—Aged 15 months; onset, October 21; paralysis in left lower limb. This patient's brother, aged 4, was taken to the doctor on account of tonsillitis and sore throat and cold on October 22. The doctor then noticed that the patient was also not well. Another brother, aged 10, was incidentally seen by me when I was called to examine Case 28. On inquiry the mother stated that the eldest boy had also had tonsillitis and had complained recently of pains in the right upper arm; some slight weakness of his right hand was found, which was confirmed at the hospital to which Case 28 had been sent. It was presumed that the eldest boy had probably had a very mild attack of poliomyelitis, and if he had not been at home when I called it is highly probable that he would have been completely missed.

*Case 20.*—Aged 16 years; onset, August 19; non-paralytic polio-encephalitis. *Case 21.*—Aged 17 years; onset, August 24; paralysis, transient ophthalmoplegia. Both these boys were in camp together with a school party from August 5–12, and were also together on August 20.

*Case 16.*—Aged 3 years 2 months; onset, July 31; left facial paralysis. *Case 18.*—Aged 5 years 10 months; onset, July 31; extensive paralysis, erector spinae group, and right and left hamstring group. These two children lived near each other and played together frequently.

*Case 9.*—Aged 11 years 11 months; onset, July 20; paralysis, legs and respiratory muscles; died, December 17. *Case 24.*—Aged 7 years 9 months; onset, July 23; bulbar paralysis, pharynx and palate, and paralysis of muscles of respiration. These two are known contacts.

*Case 10.*—Aged 3 years 11 months; onset, July 26; non-paralytic. Case 10 is not a known contact, but all the last five cases—that is, Cases 16, 18, 9, 24, and 10—although in three roads, lived practically within a stone's throw of each other.

In connexion with Case 9, the father had a cold on July 22, the mother had a cold on July 15 and diarrhoea on July 24, and a young sister had a cold on July 20.

In 1950 there was only one probable familial infection, although the possibility is also suggested in respect of the family of Case 9. However, there were three pairs of known close contacts, and two of these pairs plus one child not definitely known to be a contact live in close housing proximity to each other. It is possible, therefore, that all these five children were direct or indirect contacts of each other.

### Some Observations on Familial and Contact Cases

Stocks (1932) estimated the ratio of subliminal attacks to every overt case notified to be 100 to 1 under endemic conditions. Benjamin (1949) estimated the ratio of 100 to 1 for the epidemic conditions of 1947, with probably a much higher endemic ratio. It is not surprising, therefore, that inquiries into the health of contacts arising out of notification may throw up instances of indefinite illness which may or may not be submerged or very mild clinical poliomyelitis. An example of the latter is Case 28 (1950), and possible instances of the former are in connexion with Case 5 (1949) and Case 9 (1950).

Symptoms mentioned in other members of these families were cold, tonsillitis, sore throat, diarrhoea, and vomiting. It was also noticed that the first symptoms mentioned in a very considerable number of all the poliomyelitis notifications inquired into were of the nature of sore throat or tonsillitis. Detailed medical examination and short-term observation of the contacts of poliomyelitis cases might throw further light on the transmission channels which produce the overt cases.

The intervals between dates of onset in familial and known contact cases varied from simultaneous onset to six days. Simultaneous infection from common sources no doubt occurred in some cases. It will be noted that with regard to the group of five cases in 1950 (Nos. 16, 18, 9, 24, and 10) the first onset was on July 20 and the last on July 31. In Cases 50 and 34 (1949), grouped together because of housing proximity only, and with no known direct contact, there was an interval of nearly six weeks between dates of onset; and similarly there was a two-months interval between Cases 5 and 54 (1949), pointing to the probability of a fortuitous locality association only in these last four cases.

A further feature worthy of comment in these familial and contact cases is the apparent similarity of the type of infection or the location of paralysis in a substantial proportion of this limited group. Thus in 1949 Cases 17 and 18 both had lower-limb paralysis; Cases 9 and 10 had meningismus and polio-encephalitis respectively; and in 1950 Cases 20 and 21 had non-paralytic polio-encephalitis and transient ophthalmoplegia; Cases 9 and 24 were both severe, with respiratory paralysis. Possibly, on the other hand, Cases 50 and 34, and 5 and 54 (1949), showed dissimilar paralyses. No deductions can be drawn from such small numbers, but in future investigations of family and contact cases attention might be given to the possibility of such association.

### Summary

Three outbreaks of poliomyelitis, including polio-encephalitis, in the Metropolitan borough of Islington in the years 1947, 1949, and 1950 are reported upon. For reasons which are not clear the attack rate for 1947 was well below the London rate, but for 1949 and 1950 it approximated to those of the county as a whole. No valid deductions can therefore be drawn for any relationship between attack rates and certain social conditions.

A low proportion (27.3%) of children under 5 years were affected in 1947. In 1949 61.3% of confirmed cases were under 5, and the beginning of the outbreak was locally more explosive than in either 1947 or 1950, when the proportion of those under 5 fell to 40%.

There was a high relative incidence of left-arm—that is, inoculated-limb—paralysis in 1949, especially in children under 2, within 9–15 days of inoculation. A similar left upper limb incidence of paralysis did not occur in 1947 and 1950. In 1949 most children under 2 were given combined A.P.T./pertussis vaccine; this was not the case in the other two outbreaks. In 1949 children given pertussis vaccine only were not affected proportionately in relation to those given the combined vaccine. To a considerably less degree, paralyses in the inoculated limb have also followed within a short time the administration of other antigens, including A.P.T. These findings confirm and emphasize the wider surveys in respect of the 1949 outbreak carried out by Geffen and by Bradford Hill and Knowelden, although the Islington findings are relatively more unfavourable to the results following the use of combined vaccine.

Familial, contact, and group cases were not a feature of the 1947 outbreak, but were noticeable in the 1949 and 1950 outbreaks. Home investigations of contacts indicate the possibility of contemporaneous illness in other members of the family or others who are in close contact, which may be of the nature of abortive or very mild poliomyelitis. It

is therefore suggested that the medical examination and short-term observation of poliomyelitis contacts might provide a more realistic picture of familial and contact incidence and give further information on the transmission channels which result in clinical poliomyelitis in a proportion of those infected with the virus.

It was noticed that in some of the contacts, whether family or otherwise, there was an apparent similarity of the type of infection or the location of paralysis. The numbers dealt with here are too small to justify deductions, but it is suggested that this is an aspect for further inquiry in future investigations of family and contact cases.

I acknowledge with thanks the co-operation of Dr. A. B. Stewart, Divisional Medical Officer, L.C.C., in providing inoculation histories of poliomyelitis cases and information on antigens used, and also physician-superintendents and other hospital medical staff for kindly sending clinical information on Islington cases admitted.

BIBLIOGRAPHY

Benjamin, B. (1949). *Proc. roy. Soc. Med.*, **42**, 53.
Bradley, W. H. (1950). *Mon. Bull. Min. Hlth*, **9**, 203.
—— and Gale, A. H. (1950). Ibid., **9**, 242.
Breen, G. E., and Benjamin, B. (1950). *British Medical Journal*, 2, 1473.
Daley, Sir A. Annual Reports, London County Council, 1947, 1949.
—— and Benjamin, B. (1948). *Med. Offr*, **80**, 171.
Gale, A. H. (1948). *Mon. Bull. Min. Hlth*, **7**, 127.
—— *et al.* (1949). *Proc. roy. Soc. Med.*, **42**, 47.
Gelten, D. H. (1950). *Med. Offr*, **83**, 137.
Hill, A. Bradford, and Knowelden, J. (1950). *British Medical Journal*, **2**, 1.
Logan, W. P. D. (1950). *Mon. Bull. Min. Hlth*, **9**, 196.
McCloskey, B. P. (1950). *Lancet*, **1**, 659.
Stocks, P. (1932). *J. Hyg., Camb.*, **32**, 219.
Sweetnam, W. P. (1949). *Proc. roy. Soc. Med.*, **42**, 54.

# IMMUNITY TO OLD AND NEW STRAINS OF INFLUENZA A VIRUS

BY

**P. N. EDMUNDS, M.B., Ch.B., B.Sc.**
*(From the Department of Bacteriology, Edinburgh University)*

In the early days of influenza serology it seemed to be established that there were several immunologically distinct strains of influenza A, so that antiserum produced by infection with one strain showed a higher antibody level to that strain than to a heterologous strain (Francis and Magill, 1935; Bodily and Eaton, 1942; Hirst, 1942).

Since then, however, the following facts have emerged: Friedewald (1943), using complement-fixation tests, found that higher titres were sometimes given by convalescent sera against the PR8 strain of influenza virus—isolated in Puerto Rico in 1934 (Brown, 1936)—than against the strain of virus isolated from the patient's throat washings. Stuart-Harris and Miller (1947) also found higher serum antibody titres against PR8 than against the A strain causing the epidemic of that time (they used haemagglutination-inhibition tests). Morgan, Barnes, and Finland (1948) found that in convalescent serum a higher antibody level was present against PR8 than against the strain causing the epidemic concerned. The tests used in this instance included haemagglutination-inhibition, complement-fixation, and egg-neutralization techniques.

The following results show a similar tendency in the case of haemagglutination-inhibition and complement-fixation tests carried out in 50 normal sera against PR8 and BAR (Barclay) strains of influenza.

The time of the investigation was the first five months of 1950. Sera were obtained from blood transfusion donors at the Royal Infirmary, Edinburgh, and were taken nine months after the 1949 (March) epidemic of influenza A. The technique of the haemagglutination-inhibition tests was that of Salk (1944), except that a final concentration of 0.25% red-cell suspension instead of 0.125%, and calcium saline as diluent, were used. The latter consisted of 0.024% $CaCl_2$ in 0.85% NaCl. For the complement-fixation tests Hoyle's (1948) method was employed, except that the antigen used was infected allantoic fluid, prepared and harvested by the method of Francis and Salk (1942), instead of infected mouse-lung suspension.

## Results

Tables I (Fig. 1) and II (Fig. 2) show the titre levels involved and Table III the distribution of sera giving different ratios.

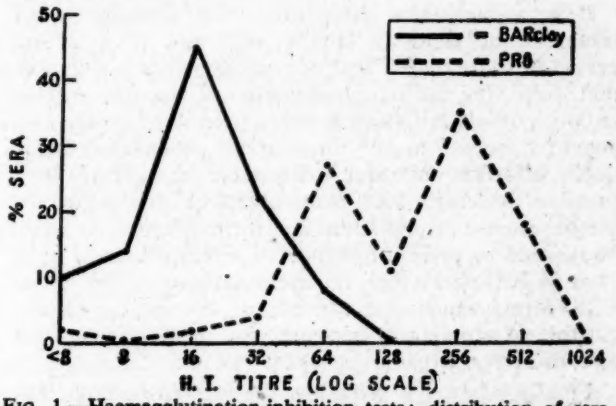



FIG. 1.—Haemagglutination-inhibition tests: distribution of sera of different titres.

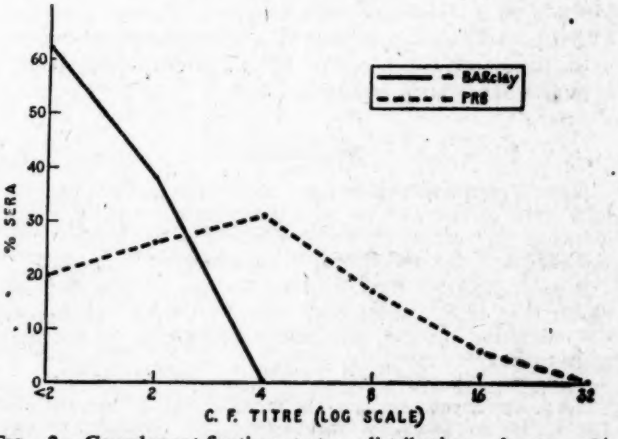



FIG. 2.—Complement-fixation tests: distribution of sera of different titres.

TABLE I.—*Haemagglutination-inhibition Tests: Percentage Distribution of Sera of Different Titres*

| Titre: | <8 | 8 | 16 | 32 | 64 | 128 | 256 | 512 | 1,024 | Total No. of Sera |
|---|---|---|---|---|---|---|---|---|---|---|
| Virus PR8 .. | 2 | 0 | 2 | 4 | 27 | 11 | 35 | 18 | 0 | 55 |
| Virus BAR .. | 10 | 14 | 45 | 22 | 8 | 0 | 0 | 0 | 0 | 49 |

TABLE II.—*Complement-fixation Tests: Percentage Distribution of Sera of Different Titres*

| Titre: | <2 | 2 | 4 | 8 | 16 | Total No. of Sera |
|---|---|---|---|---|---|---|
| Virus PR8 .. | 20 | 26 | 31 | 17 | 6 | 54 |
| Virus BAR .. | 62 | 38 | 0 | 0 | 0 | 45 |

TABLE III.—*Distribution of Sera Giving Different Ratios:* $\frac{PR8\ Titre}{BAR\ Titre}$

| Ratio: PR8 Titre / BAR Titre | ½ or less | 1 | 2 | 4 | 8 | 16 | 32 | Over | Total No. Sera |
|---|---|---|---|---|---|---|---|---|---|
| Percentage of sera (using haemagglutination-inhibition tests) .. .. | 2 | 2 | 11 | 19 | 23 | 23 | 8 | 1 | 47 |
| Percentage of sera (using complement-fixation tests) .. | 6 | 23 | 34 | 29 | 4 | 4 | 0 | 0 | 46 |

*Note.*—Titres are expressed as the reciprocal of the final dilution at the end-point. These figures are obtained using the assumption of a titre of 1 for any titre less than 2.

The average PR8 titre is 215 (H.I.T.) and 4.3 (C.F.T.), and the average BAR titre 20.0 (H.I.T.) and 1.4 (C.F.T.). The ratio $\frac{\text{average PR8 titre}}{\text{average BAR titre}} = 10$, for haemagglutination-inhibition tests, and 4, for complement-fixation tests.

It is unlikely that these high PR8 antibody levels represent the result of contact with this virus at any period of more than a year or two ago, since it is known that, following the initial response to infection, specific antibody levels fall steadily over a period of one to two years by from 5 to 100 times in the absence of subsequent infection (cf. Stuart Harris *et al.*, 1938). It is possible that high PR8 titres might be maintained by the persistence of that strain in a form in which it cannot be isolated by present methods. Current strains of virus such as BAR may then represent variants of this latent PR8 form, which are capable of causing epidemics, capable of growing in eggs or infecting ferrets or mice, and therefore capable of being isolated.

Finally, and most probably, the present findings may be taken as falling into line with the work quoted earlier, especially that of Stuart-Harris and Miller (1947) and Morgan *et al.* (1948), leading to the conclusion that the PR8 antibody levels represent a non-specific response to infection or subinfection by a current virus strain, of which BAR is an example.


## Summary

Haemagglutination-inhibition and complement-fixation tests were carried out on 50 normal serum samples, using influenza A strain PR8 (classical) and BAR (recently isolated), and the titres against these strains compared.

It was found that PR8 titres were on the average 10 times higher than titres against BAR virus by the haemagglutination-inhibition method, and four times higher by complement-fixation.


Acknowledgments are due to Professor T. J. Mackie and Dr. R. H. A. Swain for their advice and criticism; to Dr. Cummings, of the Blood Transfusion Service; and to blood donors for their co-operation in the supply of sera.

### REFERENCES


Bodily, H. L., and Eaton, M. D. (1942). *J. Immunol.*, **45**, 193.
Brown, H. W. (1936). *Amer. J. Hyg.*, **24**, 361.
Francis, T., jun., and Magill, T. P. (1935). *J. exp. Med.*, **62**, 505.
—— and Salk, J. E. (1942). *Science*, **96**, 499.
Friedewald, W. F. (1943). *J. exp. Med.*, **78**, 347.
Hirst, G. K. (1942). Ibid., **75**, 49.
Hoyle, L. (1948). *Mon. Bull. Minist. Hlth, Lond.*, **7**, 114.
Morgan, H. R., Barnes, M. W., and Finland, M. (1948). *J. Lab. clin. Med.*, **33**, 1212.
Salk, J. E. (1944). *J. Immunol.*, **49**, 87.
Stuart-Harris, C. H., Andrewes, C. H., and Smith, W. (1938). *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 228.
—— and Miller, M. H. (1947). *Brit. J. exp. Path.*, **28**, 394.


# PRESENCE OF CERTAIN SEROLOGICAL TYPES OF BACT. COLI IN THE HUMAN INTESTINE


BY

**W. W. WALTHER, M.B., B.S.**

**With the Technical Assistance of**

**E. G. MILLWOOD, F.I.M.L.T.**

*(From the Area Pathological Laboratory, Whipps Cross Hospital, London, E.11)*


Stevenson (1950) demonstrated the presence of *Bact. coli* D433 in the faeces of adults suffering from diarrhoea, but suggested that these organisms might be the normal inhabitants of the duodenum or jejunum and be carried down by increased intestinal activity due to other causes. This suggestion clearly required further study. Accordingly, during the period July 21 to October 30, 1950, swabs were taken from various parts of the alimentary tract of 51 cases (50 adults and a child of 7 months) examined *post mortem*, none of which had recently had diarrhoea or any treatment likely to interfere with the natural intestinal flora. These swabs were examined for the presence of *Bact. coli* of serological types D433, Aberdeen $\beta$, E893, E990, Vincent, and E611. Each swab was plated on half a Petri dish containing McConkey's agar medium and incubated aerobically at 37° C. for 18 to 24 hours. A comprehensive sample of the resulting growth was taken by sweeping a platinum loop across the surface of the medium, and this was first tested with a 1 in 500 solution of acriflavine in physiological saline.

Joan Taylor (personal communication) has found that some strains of *Bact. coli* other than D433 may be agglutinated on a slide by the specific sera prepared against *Bact. coli* D433, but most of these are also agglutinated by the acriflavine solution. On the other hand, none of the many strains so far examined that belong to the serological types which were the subject of this inquiry have ever been found to agglutinate in acriflavine. The acriflavine test is therefore very useful for preliminary "screening."

If no agglutination resulted in the acriflavine solution 12 individual colonies were tested with D433 K, Aberdeen $\beta$ K, and a composite serum containing agglutinins to strains E893, E990, Vincent, and E611. If agglutination occurred in the acriflavine solution some four to six individual colonies were tested with the specific sera and a further sweep was subcultured on to plain nutrient agar. Those colonies which agglutinated in any of the specific sera were also subcultured to find if they should become acriflavine-negative. This routine was repeated on the following day, when only "acriflavine-negative" colonies were tested with the specific sera, at least 12 such colonies from each agar plate being tested before the swab was pronounced "negative." The slide-agglutination technique was used throughout.

The results are summarized in the Table.

The following is a list of the conditions from which the patients died: coronary thrombosis (6), carcinoma of the lung (5), congestive cardiac failure following hypertension (5), bronchopneumonia (5), haematemesis (3), carcinoma of stomach (3), senile myocardial degeneration (2), chronic nephritis (2), carcinoma of oesophagus (2); and one from each of the following: pyonephrosis, renal failure, carcinoma of breast, carcinoma

| Agglutinin | Duodeno-jejunal Junction | | Ileum | | Transverse Colon | |
|---|---|---|---|---|---|---|
| | + | − | + | − | + | − |
| Acriflavine .. .. | 21 | 30 | 22 | 29 | 24 | 27 |
| Acriflavine negative after subculture .. | 16 | | 15 | | 15 | |

| | + | − | + | − | + | − | + | − | + | − | + | − |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| D433 K .. .. | 0 | 16 | 0 | 30 | 0 | 15 | 0 | 29 | 0 | 15 | 0 | 27 |
| Aberdeen β K .. | 0 | 16 | 0 | 30 | 0 | 15 | 0 | 29 | 0 | 15 | 0 | 27 |
| Composite E893, E990, Vincent, E611 K .. | 0 | 16 | 0 | 30 | 0 | 15 | 0 | 29 | 0 | 15 | 0 | 27 |

+ Indicates agglutination. − Indicates no agglutination.

of rectum, carcinoma of liver, lymphosarcoma, chromophobe adenoma of pituitary, senile pulmonary tuberculosis, mitral stenosis, cor pulmonale, pulmonary abscess, cerebral abscess, multiple pulmonary infarction, pyelonephritis, peritonitis, aortic aneurysm, cerebral thrombosis, and osteogenesis imperfecta.

### Summary

Swabs taken from the duodeno-jejunal junction, the ileum, and the transverse colon at post-mortem examination of 50 adults and one infant failed to provide any evidence of the presence in them of the serological types of *Bact. coli* D433, Aberdeen β, E893, E990, Vincent, and E611.

We are grateful to Dr. Joan Taylor for much helpful advice and criticism and for supplying the specific sera and the acriflavine solution.

REFERENCE

Stevenson, J. S. (1950). *British Medical Journal*, **2**, 195.

# Medical Memoranda

## Pyrexia of Unusual Origin

One of the principles of medicine is to avoid multiple diagnoses whenever possible. Thus it is particularly satisfying to be able to supply one diagnosis which satisfactorily explains a series of illnesses previously considered to be quite unrelated to one another. The case described below illustrates this point. The history was obtained partly from the patient and partly from her medical records; consequently some of the evidence is hearsay and not completely conclusive. However, I think it is convincing enough to be of interest.

### Case Report

The patient was the only child of divorced parents, both of whom had remarried and subsequently had further children. She was brought up in a convent and was studious and retiring. She felt unwanted and unloved. After failing a university scholarship examination she had a nervous breakdown and was treated with electric convulsion therapy and possibly with some form of insulin therapy. She joined the A.T.S. in August, 1947.

In December, 1947, while in a military hospital for a septic finger, she developed abdominal pain, for which her appendix was removed. The pathology was found to be inconsistent with the symptomatology. She was later suspected of tampering with her wound and creating a temperature by illicit means. She was interviewed by a psychiatrist, who considered discharging her from the Army but recommended her retention because of her unsatisfactory family background. "Psychopathic personality with emotional abnormality" was diagnosed, and she returned to duty as a medical orderly in an M.I. room.

In April, 1948, she entered a second hospital with erythema nodosum and another septic finger. She developed jaundice, diagnosed as infective hepatitis, a few days later. One month later, two days after a tooth extraction, she developed enlarged lymph nodes, "a blood picture suggestive of glandular fever and a strongly positive Paul–Bunnell." She next had whooping-cough, followed on June 26 by maxillary sinusitis. Some three weeks later she had a swelling over the right parotid gland and an abscess in the right thigh from which *Bact. coli* was cultured. A hard nodule from the region of the right knee was excised, and sections showed "fibrosis with many fat phagocytes, suggesting that trauma had played a part in its origin." She was discharged on sick leave in September, 1948.

On October 17 the patient was admitted to the Royal Victoria Hospital, Netley, with a cellulitis of her right thigh. This was treated with penicillin and sulphathiazole, and it subsided without incision. An evening pyrexia of 101–102° F. (38.4–38.9° C.) with severe night sweats persisted, and she complained of pain in her knees and ankles. By November 6 examination revealed no abnormality whatsoever except for some small scars on her fingers, thighs, and lower legs—residua from old abscesses. However, she remained febrile, and, though she was watched closely, there was no evidence that she was falsifying her temperature. *X*-ray examination of the chest, blood cultures, Wassermann and Kahn tests, catheter specimen of urine, and examination of the stools for pathogens were negative. The E.S.R. was 6 mm. in 1 hour; haemoglobin, 13.7 g. per 100 ml.; leucocytes 5,700 per c.mm. (neutrophil polymorphs 39%, lymphocytes 55%). The Widal agglutinations were:

| | |
|---|---|
| Typhoid .. .. .. | "O" 1:320; "H" 1:1,280 |
| Paratyphoid A .. .. | "O" 1:80; "H" 1:1,280 |
| Paratyphoid B .. .. | "O" 1:320; "H" 1:1,280 |
| Typhoid Vi antigen .. | 1:12 |
| *Br. abortus* and *melitensis* | negative |
| Paul–Bunnell .. .. | 1:128 |

Although there was no superficial lymphadenopathy and the spleen was not palpable, it was considered that her glandular fever was running an unusually prolonged course. We were unable to explain the Widal reaction, as she stated, and this was confirmed by her paybook, that she had never been inoculated.

On November 22 a parcel arrived at the unit for redirection to the patient. The circumstances were peculiar and suspicious. The parcel was opened and contained a syringe, needles, and numerous empty tetanus toxoid bottles. When taxed with this she admitted that over a period of some three years she had been taking various unspecified tablets and inoculating herself with tetanus toxoid and T.A.B., partly as an innocent experiment and partly in a desire for self-mortification. She admitted producing many, but not all, of the curious bumps found at the second hospital and diagnosed as erythema nodosum. She denied any malicious intentions, but felt that there must be something wrong with her head to make her behave like this, and, although depressed, she welcomed treatment.

In May, 1949, following treatment, she was well, was working, and had made a good social recovery.

### Comment

The chief interest in this case lies in attempting to assess to what extent this patient's many symptoms can be attributed to her repeated self-inoculation.

Glandular fever was diagnosed at another hospital on the strength of enlarged lymph nodes, "a blood picture suggestive of glandular fever and a strongly positive Paul–Bunnell." Glandular fever cells were not specifically mentioned, and it is not known what technique was used for the Paul–Bunnell test. It has been shown that the agglutinin in glandular fever is absorbed by ox cells but not by guinea-pig's kidney, while the agglutinin of serum sickness is absorbed by both (Stuart, Welch,

Cunningham, and Burgess, 1936). The patient at that time was thought never to have received horse serum, and so the guinea-pig's kidney absorption test may not have been performed and a false positive result accepted. While, of course, one cannot prove that she did not have glandular fever, I think the balance of evidence is in favour of a prolonged serum sickness. This is supported by the presence five months later of fever, joint pains, lymphocytosis, and a Paul–Bunnell reaction of 1:128. Unfortunately, at that time we had no guinea-pig's kidney and so could not do the absorption test. There is no history of urticaria.

It is tempting to believe that the "infective hepatitis" was really a homologous serum jaundice due to the use of an infected needle and that her "acute appendicitis" was due to mesenteric adenitis or hysterical abdominal pain. The abscesses resulted from self-mutilation; and her own story, confirmed by the biopsy of a skin nodule, suggested that the "erythema nodosum" was the result of self-inflicted lesions. The whooping-cough may have been genuine, but even this can be closely simulated by a paroxysmal cough due to enlarged mediastinal glands.

Thus, in a little less than a year, a patient suffered a series of illnesses which at first sight appeared to be quite unrelated, but which were found to have a common origin in repeated self-inoculation.

I wish to thank Colonel F. T. Escritt, Officer Commanding the Royal Victoria Hospital, Netley, for permission to publish this case.

J. W. LAWS, M.B., Ch.B.,
Formerly Captain; Graded Physician, R.A.M.C.

REFERENCE

Stuart, C. A., Welch, H., Cunningham, J., and Burgess, A. M. (1936). *Arch. intern. Med.*, **58**, 512.

## Absorption and Excretion of Pheniodol

Iodine-containing contrast agents for use in radiology should be stable in the sense that they should not yield inorganic iodine to the tissues; for cholecystography they should also be excreted in the bile. "Biliselectan" (α-phenyl-β- (4-hydroxy-3:5-diiodophenyl) - propionic acid) was introduced in 1940 (Dohrn and Diedrich) for peroral use, with the claim that it possessed both these properties. This claim would seem to have been justified by the extended use of the compound and the fact that it has received an official British name, pheniodol. Nevertheless, there are few quantitative data on its absorption and excretion, apart from some early work of Junkmann (1941).

Admittedly, experiments with laboratory animals can give no more than presumptive evidence of the behaviour of a substance used in human treatment, but the difficulties of carrying out metabolic experiments on patients led us to attempt to examine the claims of Dohrn and Diedrich by studying the absorption and excretion of pheniodol in rats and cats, making use of the "labelling" technique with radioactive iodine ($I^{131}$).

Single doses of pheniodol, equivalent to between 50 and 74 mg. per kg. of body weight, were administered by one of three routes—oral, subcutaneous, or intravenous—to pairs of rats, the excretion of iodine being studied during three-day periods by measurement of radioactivity. Single doses at about the same relative level were also injected intravenously or intraduodenally into cats under chloralose anaesthesia; in these animals the total iodine in blood, urine, and bile was measured for six-hour periods and the proportion of iodine present in organic combination was also determined by means of a butanol extraction procedure. The results are summarized in Tables I and II.

TABLE I.—*Excretion of Iodine by Rats Three Days After a Single Dose of Pheniodol*

| Excretion Route | Oral Dose | | Subcutaneous Dose | | Intravenous Dose | |
|---|---|---|---|---|---|---|
| | A | B | A | B | A | B |
| Urine .. | 25 | 78 | 20 | 80 | 33 | 82 |
| Faeces .. | 49 | 90 | 38 | 92 | 53 | 92 |

A, Total iodine as percentage of iodine in dose. B, Organic iodine as percentage of iodine in sample.

TABLE II.—*Excretion of Iodine by Cats Six Hours After a Single Dose of Pheniodol*

| Excretion Route | Intraduodenal Injection | | Intravenous Injection | |
|---|---|---|---|---|
| | A | B | A | B |
| Urine .. .. | 9 | 60 | 33 | 66 |
| Bile .. .. | 36 | 84 | 20 | 87 |

A, Total iodine as percentage of iodine in dose. B, Organic iodine as percentage of iodine in sample.

It will thus be seen that in rats little inorganic iodine is liberated from pheniodol administered by any of three routes, and that after oral or intravenous dosage nearly all the iodine was eliminated in the urine and faeces by the end of 72 hours; examination of the curves of excretion show that further small quantities would have been eliminated subsequently. Further, it is clear that the small amount of iodine eliminated as inorganic salts was rapidly excreted by the kidneys. Similarly, in cats a large proportion of the compound was eliminated during the first six hours after intravenous and intraduodenal administration, and in these animals also any breakdown of the compound was effectively handled by their excretory mechanism. In the cats rapid passage of the compound into the bile is also evident. It is of interest to note that experiments on a single pregnant cat indicated that the compound cannot pass the placental barrier.

Therefore, so far as experiments with rats and cats permit valid extrapolation to human patients, the work summarized above, of which it is hoped to publish full experimental details elsewhere, gives support to Dohrn and Diedrich's claims to have brought forward a satisfactory cholecystographic agent.

AUDREY A. FREE, B.A.
J. E. PAGE, B.Sc., Ph.D., F.R.I.C.
E. A. WOOLLETT.
Glaxo Laboratories Ltd., Greenford, Middlesex.

REFERENCES

Dohrn, M., and Diedrich, P. (1940). *Dtsch. med. Wschr.*, **66**, 1133.
Junkmann, K. (1941). *Klin. Wschr.*, **20**, 125.

The report for 1950 on the work of the rheumatism department of the Royal Free Hospital shows that rheumatoid arthritis was by far the commonest diagnosis (42%) among the in-patients. Ankylosing spondylitis and osteoarthritis were each found in 12% of the patients admitted during the year, and 7% suffered from prolapsed intervertebral disk. Multiple diagnoses were not uncommon, especially in the old patients. Follow-up records have been kept, and a relatively high number of patients discharged from the hospital have been kept under review.

# Reviews

## ANTICOAGULANTS

*Thromboembolic Conditions and their Treatment with Anticoagulants.* By Charles D. Marple, M.D., and Irving S. Wright, M.D. (Pp. 418; 27 illustrations. £3 3s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1950.

Since the isolation of the active principles of heparin by Best and his colleagues in 1937, and of dicoumarol by Link and his associates in 1940, the literature on the uses and abuses of anticoagulants has grown to almost unmanageable proportions. Drs. Irving Wright and Marple have surveyed this mass of material and have presented a comprehensive and readable book on the uses of anticoagulants in the many different kinds of thromboembolic condition. It sets out clearly the rationale and the theories underlying anticoagulant therapy. In Britain dicoumarol is used with considerable hesitation, both in cases of cardiac infarction and in venous thrombosis, partly because of the necessity for regulating the administration of the drug by frequent prothrombin estimations, and partly from fear of the massive haemorrhages which have been reported from time to time in cases that appeared to be unusually sensitive to this drug. This book should reassure the hesitant, since it offers many practical suggestions for the treatment of difficult cases. The authors can write authoritatively on their subject, for they not only know of the experiences and difficulties of others, but have also contributed notably to the knowledge of the uses and control of anticoagulants in laboratory and clinic.

The book is well set out, subdivided into short chapters for convenient consultation, and contains nearly seven hundred references to original articles. It should prove of great value to the clinician who is in doubt whether anticoagulant therapy is suitable for a particular patient, while to those who are already working on problems of thromboembolism it offers a stimulating critical review of the statistics and papers published on this subject up to the end of 1949. It is regrettable that in a review book such as this the method of referencing is by serial numbers and not alphabetically. To find a reference again the author of which is known, the reader must go through the whole text, and, since such an author may be cited in one of several chapters, this may mean a protracted search. A second edition would be much improved either by using the Harvard system for the bibliography or by the inclusion of an alphabetical author index.

It is a book which can be recommended with every confidence to practitioners in medicine, surgery, or obstetrics, while to the pathologist, who must advise his clinical colleagues on the uses of anticoagulants, it will prove of the greatest value.

H. PAYLING WRIGHT.

## INFECTIOUS FEVERS

*Modern Practice in Infectious Fevers.* Edited by H. Stanley Banks, M.A., M.D.(Glas.), F.R.C.P., D.P.H. Volumes 1 and 2. (Pp. 989; 209 figures. £5 set of two volumes.) London: Butterworth and Co. 1951.

Does the work expound its title? Perhaps not quite. This is a symposium. The general editor has invited (including himself) fifty-two contributors of unimpeachable credentials to survey the whole field of infectious diseases, including protozoal and mycological infections, in a thousand pages less those liberally given to illustration. Had powers of concentration surpassing the gnomic utterance of a Francis Bacon been available they would hardly have sufficed for this task.

Here many facts are reduced to a state of severe dehydration; many others, familiar doubtless to the expert though useful to the unspecialized, have had to be omitted, and, despite editorial claims, it is nearly always the clinician who gets served worst. For instance, Dr. Banks in the one paragraph he allots to laryngeal diphtheria dismisses tracheotomy—that eminently practical procedure—in five short, not very useful, sentences, omits aftercare, mentions no operative complication, and, while admitting the existence of scarlatinal nephritis, does not discuss management of a case. Already the section devoted to treatment of tuberculous meningitis needs expansion and rejuvenation. Against this, bacteriologist and serologist are less severely curbed.

The text is sprinkled with references to papers published between 1930 and 1950, and if one suspects that the confident claims of 1949 will be superseded by those of 1952 that is perhaps inevitable nowadays.

In effect here is rigorous scientific stuff assembled for teacher rather than student, library rather than study. Certainly there is much remarkable news from field and laboratory alike and far more information than can be properly assessed by any one mind. The work merits, what it must receive, a place in every reputable centre. But, while it would be absurd not to applaud the diligence and skill that have gone to its making, your reviewer cannot but regret that too seldom are we permitted to see (as Dr. Laurent so well shows us) the patient as a human being sick in his bed and not as an aggregate of colloids undergoing complex transformations, whose *raison d'être* is to be jabbed with a needle and put on a list. But science and humanity are drifting apart. Facts are becoming utterly brute. The very notion of mind is (we learn from Oxford) just a superstition.

Austerity does not mar this sumptuous treatise. Binding, paper, type, lay-out, and illustrations are well above average. As book-craft these weighty tomes can stand unashamed on the shelf beside the best American work. Even the price is not too daunting. Perhaps a separate index to Volume 1 would have been useful, for the books might get parted.

JOSEPH ELLISON.

## CYTOLOGY OF VAGINA

*Cytology of the Human Vagina.* By Inés L. C. de Allende, M.D., and Oscar Orias, M.D. Foreword by Bernardo A. Houssay, M.D. Translated from the Spanish by George W. Corner, M.D. (Pp. 286; illustrated. £2 15s.) London: H. K. Lewis. 1950.

Interest in vaginal smears has recently been focused on their use in the early diagnosis of cancer of the uterus. The consequent tendency to overlook their other uses, which, even if less practical, are by no means negligible, is here remedied. This book begins with a clear account of the normal histology of the vagina, and of variations in its exfoliated cells according to age and ovarian activity. The authors then describe smear studies as a method of diagnosis in cases of menstrual disturbance, anovulation, and sterility, and as a means of controlling hormone therapy.

Dr. de Allende learned the staining techniques in the Carnegie Institute in Baltimore, and has since worked

for five years at Cordoba under the direction of Professor Orias. The findings in many respects are not new, and they serve rather to confirm and elaborate those of earlier workers. But it is convenient to have the data assembled and presented in this attractive form by authors who write with authority and a wide background of experience. The details of the method for collecting and staining vaginal debris are particularly well described, and the reproductions of microphotographs are excellent. The fact that anyone of the standing of Dr. G. W. Corner should have been responsible for the English translation is in itself high praise. The subject is one with a strictly limited scope, and is here made to extend over 286 pages only by a good deal of repetition. The authors clearly recognized this shortcoming, but apparently found it difficult to correct.

T. N. A. JEFFCOATE.

## LOOKING BACK

*Pioneer Doctor.* By Lewis J. Moorman, M.D. (Pp. 252. $3.75). Norman, Oklahoma: University of Oklahoma Press. 1951.

This is a medical variant of the familiar story of boy from small town who made good. It is interesting not only because of the hard and exciting way in which Dr. Moorman made good, but to one reader at any rate for the emphasis which a well-known specialist places on the value of the training he got as a general practitioner. The story of his early days shows how primitive were the conditions in the West only 50 years ago. With a medical companion the author joined up with a crowd of land-seekers on their way to El Reno, where there was to be a lottery with free land as prizes. They had no luck in the lottery, but their experience is reminiscent of "gold rush" stories in various parts of the world. The two of them then put up a sign in a small town and waited two months for patients—total income two dollars. They moved on, and eventually Dr. Moorman settled at a town named Jet, where he spent six exciting and obviously happy years as a "horse and buggy doctor."

At the end of that time, being anxious to improve his medical experience, he went into partnership with a doctor in Kentucky who was a skilled paediatrician. He then set up for himself in Oklahoma City, where after the usual boring waiting for patients he became attached to a hospital associated with the struggling young medical school. He found that "the best way to learn is by teaching." In 1909 he went to Vienna for a year's postgraduate work. He has some interesting things to say about the medical celebrities of that school. Though appreciative of their learning and skill, he got the impression that they were more interested in diagnosis than in the welfare of the patient, and this clashed with all his ideals as a general practitioner.

On his return home he found himself becoming specially interested in tuberculosis, and founded "an elementary sanatorium." From then onwards he became, almost despite himself, a specialist. Some of the best chapters of his book are devoted to various aspects of the disease and its sufferers. He gives a list of victims of it who have made memorable contributions to history. Dr. Moorman, together with Osler, Welch, Trudeau, and others, was a founder of the American National Tuberculosis Association and a prominent figure in every movement connected with it. He is cautious in his pronouncement about the value of the antibiotic drugs and says, "Conservative physicians who know a lot about T.B. realize that patience and perseverance are perhaps the most important ingredients in any research programme having to do with this disease."

There are many kindly references to medical notabilities with whom the author has associated. In summing up his experiences as a general practitioner, a teacher for 20 years, and a former dean of his medical school, he says he thinks that in the pursuit of the science of medicine "we have suffered a distinct loss in the art." He has much of value to say about medical education, and believes that most of medical teaching "should be done by physicians in general practice who see the people in complete cross-section." I can cordially recommend this book to all interested in medical education and the social tendencies of our time, and not less to those who like to read exciting and humorous experiences of a "Pioneer Doctor."

ALFRED COX.

## BOOKS RECEIVED

*Review is not precluded by notice here of books recently received*

***A Guide to the Fishing Inns of Scotland.*** Compiled by R. Crombie Saunders. (Pp. 118. 9s. 6d.) London: Nicholas Kaye. 1951.

***Textbook of Obstetrics.*** By J. F. Cunningham, M.D., M.A.O., F.R.C.P.I., F.R.C.O.G. (Pp. 499. 40s.) London: William Heinemann. 1951.

***The Vitamin B Complex.*** By F. A. Robinson, M.Sc., LL.B., F.R.I.C. (Pp. 688. 60s.) London: Chapman and Hall. 1951.

***A History of Medicine: Primitive and Archaic Medicine.*** By H. E. Sigerist, M.D., D.Litt., LL.D., Dr.h.c. Vol. 1. (Pp. 564. 45s.) London: Geoffrey Cumberlege. 1951.

***Modern Practice in Infectious Fevers.*** Edited by H. S. Banks, M.A., M.D., F.R.C.P., D.P.H. Vols. 1 and 2. (Pp. 989. 100s. per set.) London: Butterworth. 1951.

***The Health of the Mind.*** By J. R. Rees, C.B.E., M.A., M.D., F.R.C.P. 2nd revised ed. (Pp. 208. 9s. 6d.) London: Faber and Faber. 1951.

***Proceedings of the First International Conference on Alcohol and Traffic.*** (Pp. 336. 15 Swedish kronor.) Stockholm: Kugelbergs. 1951.

---

An exhaustive *Classified Bibliography of Gerontology and Geriatrics, 1951*, has been prepared for Stanford University, California, by Dr. Nathan W. Shock. In its 600 pages are contained over 18,000 references to books and papers on every aspect of the subject, including the biological, physical, and clinical problems associated with ageing. The bibliography is world-wide in scope, and is arranged under broad subject headings according to systems and organs. It covers the literature up to the end of 1948; supplementary references on the subject are now published regularly in the *Journal of Gerontology*. References to journals are abbreviated according to the rules of the *World List of Scientific Periodicals*. Author and subject indexes are provided, together with a list of about 2,400 journals cited and the abbreviations used for them. Modern geriatrics may be said to start with Sir John Floyer's classical *Medicina gerocomica*, or *The Art of Preserving Old Men's Health*, 1724. Unfortunately, the compiler gives an incomplete and inaccurate reference to this important work, although it is preceded by an accurate reference to the second edition (1738), which should have aroused his suspicion. But the book is well arranged and produced, and like all good bibliographies will be of permanent value. Its production was made possible by a grant from the Forest Park Foundation, Peoria, Illinois, and it is published by the Stanford University Press at $15.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JULY 21 1951

## THE AETIOLOGY OF ATHEROSCLEROSIS

In his famous treatise on diseases of the arteries Sir Clifford Allbutt[1] described under the term "senile or decrescent sclerosis" those types of arterial degeneration which later became known as arteriosclerosis. It is unfortunate that for many years afterwards there was an apathetic and unjustified tendency to regard arteriosclerosis as an inevitable result of ageing. In more recent years it has become apparent that the reverse is probably more true: nearly all the symptoms and signs of senility are directly caused by tissue ischaemia secondary to local or generalized arterial narrowing.[2] In short, it still remains fairly true to say that a man is as old as his arteries, but not that the arteries are as old as the man. If it is accepted that arterial degeneration is a disease process and not merely a manifestation of senility, then surely it is a disease worthy of our closest attention, since it accounts not only for many tragic and untimely deaths in middle age from the complication of coronary thrombosis, but also for the cerebral complications which are so often responsible for irrecoverable and helpless invalidism in old age.

The term arteriosclerosis is one which no longer has any precise meaning. It has come to embrace three distinct types of arterial disease: diffuse hyperplasia of the arterioles, fibrosis and calcification of the arterial media, and atherosclerosis. Of these, it is atherosclerosis which is largely responsible for the cardiac and cerebral disasters of ageing man. In the opening pages of this issue Dr. J. B. Firstbrook reviews some recent work on the pathogenesis of atherosclerosis. He considers that the incidence of the disease increases with age because the lesions are slow to develop, and because many diseases which predispose to atheroma, such as obesity and diabetes, are more common in older people. However, the occasional finding of advanced atheroma in childhood and the complete absence of atheroma in some very old people show that other factors besides age must operate. Since it was discovered that atheromatous lesions in man contain large amounts of cholesterol much experimental evidence has been adduced to suggest that abnormalities in cholesterol metabolism may play some part in the development of atherosclerosis. Not only is there a high incidence of atherosclerosis in those diseases associated with hypercholesterolaemia, but the serum cholesterol has been found to increase with age in normal people and to be higher in men with coronary atheroma than in controls. It is known that certain races living on diets low in cholesterol show a remarkably low incidence of atherosclerosis, and the fall in the number of deaths from circulatory disease in Scandinavia during the second world war has been attributed to a diminution of dietary fat during that period.[3,4]

Laboratory experiments support the view that faulty cholesterol metabolism is associated with atherosclerosis; true atheroma can be reproduced only in animals if cholesterol is administered by mouth or by injection, and the amount of atheroma bears a fairly constant relationship to the duration and extent of the hypercholesterolaemia. Obesity is another factor which statistics have shown to predispose to atherosclerosis and cardiovascular disease. Firstbrook describes his experiments on rabbits in which he was able to show that the advent of atheromatous lesions in cholesterol-fed animals can be delayed or inhibited by preventing the animals from gaining weight. In man, however, obesity is a complex factor; it often results from over-eating, and it is commonly associated with hypertension, which in itself is an aggravating cause of atherosclerosis. Firstbrook concludes that there is good evidence to suggest that a diet low in animal fat may prove of value in the prevention of atherosclerosis.

Whatever the importance of disordered cholesterol metabolism, it is necessary to remember that fat deposition is a relatively late finding in atheromatous lesions. The earliest change consists in a fibrous thickening of the intima, and it is usually assumed that this is brought about by proliferation of the intimal endothelium. However, Duguid recently reported a series of observations which casts some doubt on this theory.[5,6] He demonstrated that thrombi in the coronary arteries sometimes undergo fibrous organization, giving rise to lesions identical to those of atherosclerosis. Similarly he showed that in the aorta small mural thrombi often form fibrinous deposits on the intimal surface; these thrombi later become covered with endothelium and incorporated in the vessel wall, where they undergo hyaline and fatty degeneration. These findings open new fields

1 *Diseases of the Arteries*, 1915, London.
2 Stieglitz, E. J., *Geriatric Medicine*, 1949, Philadelphia.
3 Malmros, H., *Acta med. scand., Suppl.* 246, 1950, p. 137.
4 Ström, A., and Jensen, R. A., *Lancet*, 1951, 1, 126.
5 *J. Path. Bact.*, 1946, 58, 207.
6 Ibid., 1948, 60, 57.
7 Ibid., 1948, 60, 413.
8 *British Medical Journal*, 1949, 2, 1343.
9 *Lancet*, 1951, 1, 1.

of research into the causation of atheroma, since, if they become accepted, the primary cause of atherosclerosis must be sought not in the vessel walls but in the blood itself. There is good evidence that rapid variations in the coagulability of the blood occur in numerous pathological conditions. Mole[7] demonstrated the presence of a circulating fibrolysin in human blood and suggested that production of fibrolysin is part of the body's reaction to injury. As we have previously commented in this *Journal*,[8] deficiency in fibrolysin with consequent formation of mural thrombi and atherosclerosis might represent a failure of the body's defence against injury, a theory which would be in keeping with the widely held belief that atherosclerosis is one of the diseases associated with the stress of modern life. There is no direct proof, however, that atherosclerosis is becoming more common; indeed, Morris[9] has shown that there is reason to believe that it may be less common. In analysing the necropsy records of the London Hospital he showed that, whereas there has been a real increase in myocardial infarction since the first world war, there has been a substantial decrease in advanced coronary atheroma. This surprising finding implies that myocardial infarction may not be the direct result of atheroma and that it may be fallacious to estimate the incidence of atherosclerosis from the number of deaths from coronary thrombosis. It is clear that much further research is needed to elucidate the many problems of the aetiology of atherosclerosis.

## NOTIFICATION OF RHEUMATIC FEVER

The deaths from rheumatic heart disease, rheumatic fever, and chorea in 1945 amounted to 15,333. In the same year the deaths from tuberculosis were about 24,000. Morbidity rates for the two diseases were probably about the same. The cost to the country, reckoned in terms of inability to work or non-productive employment of fit people in looking after the invalids, is not easily assessed, but it is probably about the same for the two diseases. Thus the rheumatic state with its sequelae is almost as great a scourge as tuberculosis in this country—a fact of which the public is not yet aware. Some believe that compulsory notification of rheumatic fever is an essential step in the battle against this disease. But those diseases which are at present notifiable by law are, on the whole, infectious diseases or diseases of occupation. Notification is necessary here, so that the danger to the unaffected members of the community may be promptly controlled. Rheumatic fever, on the other hand, is neither infectious nor a disease of occupation in the ordinary sense of these terms, and the case for its compulsory notification is somewhat different. In putting this case Ryle[1] rested upon one main premise, that there was a relationship between social conditions and rheumatic fever: for example, in 1927 Still had asserted that "rheumatism . . . is a disease which affects but rarely the children of the well-to-do; its incidence is chiefly on the poorer class."[2] Shortly after the appearance of Ryle's paper the Ministry of Health inaugurated compulsory notification in three trial centres—Bristol, Sheffield, and the Lincolnshire-Grimsby-Hull area. Since then two other arguments for compulsory notification of rheumatic fever have been put forward. The first of these is based on the evidence that chemoprophylaxis of streptococcal infection, especially in known rheumatic subjects, will greatly decrease the incidence of recurrences of rheumatic fever.[3,4] If children have more than one attack of rheumatic fever they rarely escape heart damage: therefore, it is argued, all rheumatic children should be notified, so that they may attend clinics where the chemoprophylaxis can be supervised. The second new reason for compulsory notification is based on the hope that cortisone can avert the changes of rheumatic valvular disease. To be most effective it should be given early, and notification, by enabling ill children to be seen promptly at specialist clinics, should ensure rapid diagnosis and treatment.

The case against compulsory notification is perhaps stronger. The results of the first three years of notification in the Sheffield area were reported by Dr. Llewellyn Roberts at a recent meeting[5] of the Royal Society of Medicine. His figures gave no conclusive support to Still's contention that rheumatic fever is a class disease. Further, the incidence of rheumatic fever in the notification areas is only 0.5 per 1,000, and, as was pointed out at the same meeting, the figure is small compared with the incidence of established rheumatic heart disease found at medical-board examinations of recruits for the Forces (39.3 per 1,000) and at mass-radiography surveys (4 per 1,000). Even if a decrease in the incidence of rheumatic fever during the last 20 years is allowed for, it is difficult not to conclude that few of those with rheumatic fever are notified or that not all rheumatic heart disease is a consequence of rheumatic fever. In fact, as Dr. J. W. Brown remarked, it is a common experience to find a patient with established rheumatic heart disease who has had no previous symptoms suggesting rheumatic fever. Even when rheumatic fever has occurred its severity is

[1] *J.R. sanit. Inst.*, 1946, **66**, 277.
[2] *Social Condition and Acute Rheumatism*, 1927, H.M.S.O., London.
[3] Thomas, C. B., and France, R., *Bull. Johns Hopk. Hosp.*, 1939, **64**, 67.
[4] Evans, P., *Proc. roy. Soc. Med.*, 1950, **43**, 206.
[5] Reported in *British Medical Journal*, 1951, **1**, 1328.
[6] Ibid., 1951, **1**, 856.

often quite unrelated to the severity of the valvular damage which follows. Thus notification could not be expected to bring for treatment many patients with mild or symptomless rheumatic carditis who are later to develop valvular disease, while patients with more severe rheumatic fever would come under medical supervision without compulsory notification. In a recent paper in this *Journal* Magarey[6] has shown that post-rheumatic thickening of mitral valves may depend on a process of fibrin deposition and organization on the surface of roughened valves. This process is found in normal hearts and is pathologically accelerated in those with rheumatic valvulitis. Once started, the thickening may be self-perpetuating; this would explain the lack of correlation between the severity of rheumatic carditis and the subsequent valvular deformity, and it also means that the "cure" of rheumatic valvulitis by cortisone will not necessarily reduce the rate of subsequent fibrin deposition upon the valve.

On the whole it would seem that notification of rheumatic fever is justified only where it serves the purpose of special research into the social background of this disease. Such research is important, though it has so far produced largely negative results. The value of notification as an adjunct to chemoprophylaxis of recurrences in rheumatic subjects is being tested on a limited scale in the Bristol area, but the results of this are not yet available.

## THE 1951 CENSUS

The Registrar-General has issued his preliminary report[1] on the 1951 census with commendable speed. The population of England and Wales was 43,744,924 persons—an increase of 3,792,547 on the 1931 census. This is the largest population ever reached in this country and represents a density of 750 persons per square mile, a density higher than that of nearly every other country in the world. The growth of the population during the intercensal period exceeded the natural increase, the excess of births over deaths. This is the first time during the past century that a gain from immigrants has been recorded; in previous census intervals there has invariably been an outward balance from emigrants. Part of the recent gain was due to the discharge into the civilian population of about 80,000 members of the Allied armed Forces who elected to remain here rather than return to their homeland.

The population contained 1,696,550 more females than males, the number of females per 1,000 males being 1,081. This ratio is markedly higher than any recorded between 1801 and 1911, but lower than the ratios of 1921 and 1931. In 1951 males predominated in the rural areas, where for every 1,000 there were 983 females, compared with 1,106 in the urban areas. An excess of females has probably become a permanent feature of the population due to the growing numbers at older ages, in which females, by reason of their lighter mortality, outnumber men by 2 to 1. The excess of females also reflects the gaps in the male population caused by the two wars. The sex distribution differs widely in different areas of the country. The greatest preponderance of females was found in the London and south-eastern counties, where the ratio was 1,136, and in the north-western region (1,108), while the lowest ratios were found in the northern region (1,039) and the north midland region (1,038). The counties with the largest excess of females were East Sussex (1,280) and West Sussex (1,234), and those with the lowest ratios were Rutlandshire (916) and Wiltshire (898).

The growth of the population varied throughout the country, but the loss of population by the northern counties and Wales to the southern counties continued. The largest percentage increases in population were 27.2 in the eastern and 24.1 in the southern regions, while the smallest increases were 0.1 in Wales and 3.3 in the northern region. Sixteen counties recorded increases in population of over 20%, the largest being those of Hertfordshire (52%), West Sussex (42.9%), Buckinghamshire (42.3%), Bedfordshire (41.4%), and Middlesex (38.4%). The only English counties with a smaller population in 1951 than in 1931 were Durham and London, with a decline of 2% and 23.8% respectively. In eight of the thirteen counties in Wales there was a small decrease, ranging from 2.2% to 6.2%. In 1951 the population of London was 1,048,667 fewer than in 1931. This tremendous loss was due to the great destruction caused by enemy action, and, as would be expected, the decline was greatest in the central and eastern boroughs, which suffered the most concentrated attacks. The largest fall in population was 56.2% in Stepney, but Shoreditch, Poplar, and the City of London lost more than half of their population; and in the four adjacent boroughs of Bermondsey, Bethnal Green, Finsbury, and Southwark the fall in population was almost as large. Only in the boroughs of Woolwich, Lewisham, and Hampstead, on the outer edge of the L.C.C. area, were there small increases. The population of Greater London (substantially the Metropolitan Police District, together with the City of London) in 1951 was 8,346,137; this was 130,464 above the total of 1931.

[1] *Census 1951, England and Wales, Preliminary Report*, 1951, H.M.S.O., London.

Birmingham has consolidated its position as the second largest city in England, with an increase of 10.9% since 1931, while its nearest rivals, Liverpool and Manchester, suffered a loss of about 8% of their previous population. Birmingham now has a population of 1,112,340, which is nearly 30,000 more than that of Glasgow, although in 1931 the population of Glasgow was more than 80,000 above the Birmingham total. There are now 156 towns with a population of 50,000 or more, compared with 113 in 1931. Extensive revision of boundaries and the amalgamation of smaller units have helped to bring about this increase in the number of large towns, most of which recorded increases in their populations. Twenty-seven had gains of 50% or more—13 of these had increases of over 100%. At the other extreme 23 towns had losses of more than 5%. Twenty-two of the 27 areas with gains of 50% or more were either in Greater London or within easy reach of the Metropolis, while the other five towns were close to large, over-populated cities. The largest decrease in the population of a large town was 41.9% in West Ham in Greater London. Four other towns (Tottenham, Leyton, East Ham, and Walthamstow) in the north-east and east of Greater London also had large decreases. Outside London the towns with the largest falls in population were Rhondda (21.2%), Salford (20.3%), and Merthyr Tydfil (14.1%). Despite the severe damage suffered by Coventry during the war the population increased by 80,085 (45%) over the 1931 total—another instance of the change brought about by the internal combustion engine.

## THE FLORA OF INFANTS' FEEDS

Dr. Joyce Wright describes on page 138 the results of examining bacteriologically the contents of 300 infants' feeding-bottles. The feeds were prepared either in hospitals (126), in residential nurseries (91), or by mothers who had brought them with the child to out-patient departments or welfare clinics (83). More than half of the feeds were made from dried milk, the remainder including liquid milk and other products. Their general bacterial content varied from *nil* to many millions of organisms per ml., and, while in a majority the count was reasonably low, it is all the more necessary to inquire why in others it should have been unduly high. The species found included no frank intestinal pathogens, and comparatively few on the borderline of pathogenicity, such as *Bact. coli* and Group D streptococci, but the presence of such organisms indicates a possibility that more serious contamination might occur. Otherwise most of the bacteria were harmless enough in themselves: only their numbers and the chemical changes resulting from their growth were likely to be harmful. There was little evidence to relate a high bacterial content with gastro-intestinal disturbance—and, indeed, to establish such a relationship was not the purpose of this study—but it seems likely from the few examples cited that heavily contaminated feeds may be badly tolerated.

Two types of feed gave particularly unsatisfactory results in view of their nature—expressed breast milk and "clear" solutions. Dr. Wright has previously shown that the bacterial content of breast milk can be reduced by over 99% when the pump and bowl used for collection are boiled. There is still less reason for heavy contamination of mere glucose solution or water: that these should be visibly cloudy from bacterial growth or betray fermentative changes by their smell is inexcusable. There should be no difficulty in ensuring that such material is completely sterile. The number of specific faults noted in connexion with the institutional preparation of feeds was no less than 16. Many of these had to do with imperfect sterilization of teats and bottles, despite the fact that these were everywhere boiled, or their contamination after sterilization, and failure to cool prepared feeds to a temperature at which bacterial growth would not occur. It is interesting that when preparation of feeds was supervised by a bacteriologist the colony counts in one milk kitchen where they had previously been high were reduced to zero.

Apart from the elimination of obvious or not so obvious errors in methods of preparation and storage of feeds the main suggestion made for improvement is the adoption of the American system of "in-bottle" sterilization of prepared feeds. This is clearly much the most efficient safeguard and removes the need for anything but simple cleanliness in previous preparation. American practice varies from simple boiling or steaming to low- or even high-pressure autoclaving. The latter is obviously undesirable, owing to its effect on the food itself. It is indeed questionable whether a temperature as high as 100° C. is worth attaining, since all except sporogenous bacteria are killed by heating for a short period at about 75° C. Presumably the widespread practice of boiling is due rather to its simplicity and certainty of effect without intelligent control than to any considered belief that anything is to be gained by raising milk much above the thermal death-point of vegetative bacteria. If any such heat treatment of prepared feeds were followed by immediate efficient cooling there is no reason why a whole day's feeds should not be prepared at one time and remain practically bacteria-free.

## REVISED HEALTH SERVICE ESTIMATES

Revised estimates for the health service, which were issued last week, show the effect of the charges for false teeth and spectacles imposed by the new National Health Service Act. The original estimates, as the Chancellor of the Exchequer explained in his Budget statement, had taken into account the savings to be derived from the charges; with the permitted increase in the hospitals' budgets, it was only by taking the charges into account that the total estimated cost of the

health service was kept within the limit of £400m. But, according to the memorandum to the revised estimates, although the charges were taken into account, it was not known exactly where they would fall. Thus the savings from the charges were spread over the three branches of the health service where charges might be expected—the pharmaceutical service, the dental service, and the supplementary ophthalmic service. Now that it is known that charges are to be imposed only for false teeth and spectacles the consequent adjustments have been made and are shown in the following table :

| Estimated Costs of: | £ million | | |
|---|---|---|---|
| | 1950–1 Final | 1951–2 Original | 1951–2 Revised |
| Pharmaceutical service .. .. | 32·0 | 34·6 | 43·6 |
| Dental service .. .. .. | 46·9 | 39·9 | 36·2 |
| Supplementary ophthalmic service | 28·1 | 18·6 | 14·6 |

The revised estimate for the pharmaceutical service deserves some comment. When the estimate for 1950–1 was drawn up it was evidently assumed that the proposed charge for prescriptions would be imposed. If this assumption had not been made, the estimate would presumably have been £10 million higher and therefore more comparable with the revised estimate for this year, which takes account of no such charge. Nevertheless the estimate of over £43 million is staggering. It compares with an actual expenditure of £35.3 million in 1949–50. The cost of the dental and ophthalmic services has fallen since 1949–50 even without the new charges—partly because of the reductions in practitioners' fees and, in the case of spectacles at least, partly because of a falling off in demand. But the drug bill continues to rise.

What will perhaps be of most interest to doctors is the total cost of the health service as shown in the revised estimate. Although it is not called a supplementary estimate—since supplementaries are ruled out—the total cost shown in it has gone up from the £398,083,000 originally presented to Parliament to £399,183,000. The rise is attributable partly to the cost (estimated at £200,000) of sending tuberculous patients for treatment abroad, which is provided for in the new National Health Service Act, and partly to an arbitration award of £800,000 to Scottish chemists. Doctors will not grudge either of these items. But they will note that, as a result, the £2m. balance offered by the Ministry for increasing capitation fees has fallen to less than £1m. Their position as residuary legatees has become absurd. By the time the working party proposed by Mr. Marquand would have reported, the balance might well have disappeared altogether.

## FOREIGN BODIES IN THE CARDIOVASCULAR SYSTEM

Recent advances in the surgery of the heart and greatly increased experience at many centres have altered some of the long-standing opinions about the treatment of foreign bodies in the cardiovascular system, and Barrett's[1] comprehensive review of the subject will prove valuable. Patients with foreign bodies retained in their hearts, as well as those in whom foreign bodies have migrated with the blood stream from part to part, have always excited the interest of surgeons, and many such stories, tall but true, are recorded, and often repeated, in medical papers and textbooks. Included among the foreign bodies are missiles of war of all kinds and many commoner objects, especially needles. Not all are radio-opaque. Many of them enter the cardiovascular system by penetrating veins, and, while this may occur immediately at the site of the wound of entry, as in limb injuries or particularly those of the liver, it sometimes happens more obscurely or is delayed. Radium needles have gained entrance to veins by a process of slow necrosis. Swallowed foreign bodies may end up in the cardiovascular system by penetrating the jugular vein through the piriform fossa, by penetrating the pericardium where it is adjacent to the lower third of the oesophagus, or by penetrating the duodenal wall and so entering the inferior vena cava. Other objects may enter the pulmonary veins. Arteries, both pulmonary and systemic, may also be entered, but much less commonly than veins, and seldom except as a result of penetrating wounds : the vessel is usually the aorta. A foreign body free in a blood vessel will commonly migrate as an embolus, but heavy objects can move with gravity against the blood stream. Impaction in a peripheral artery may cause gangrene or a cerebral lesion. Objects which have entered veins usually reach the heart and may lodge in one of its chambers or pass straight through and rest in a branch of a pulmonary artery. Migration may occur intermittently, and paradoxical embolism has occurred in patients with a patent foramen ovale. Sepsis may be a serious complication, for organisms or pus in adjacent blood clot or clothing fragments can cause pyaemic abscesses. Although some foreign bodies in the heart reach it by embolism, direct entry is more common—for example, by an unsuccessful attempt at suicide with a needle. Such objects have often been reported to have remained in the heart for long periods, apparently causing no harm, but dangerous complications are also common. Some of these, such as haemorrhage, tamponade, or infection, occur early; others, such as aneurysm, thrombosis, or embolism, are delayed even for many years. Foreign bodies which have entered a chamber of the heart tend to migrate, but they may become encapsulated in a mural clot, and during this process fragments of the clot may themselves form dangerous emboli. From the right ventricle foreign bodies migrate to the pulmonary artery, but they do not cause infarction of the lung, though, if infected, they can cause an abscess. Barrett concludes that, in general, a foreign body lodged in the heart should be removed. This conclusion, though different from that of a number of surgeons in previous decades, is the same as that reached by Harken,[2] who had a wide experience of heart surgery during the last war. The operation, which should be done only under ideal conditions, is particularly indicated when the injury is fairly recent, when the object is jagged or likely to be infected, and when it is within a chamber of the heart.

[1] *Brit. J. Surg.*, 1950, **37**, 416.
[2] *Surg. Gynec. Obstet.*, 1946, **83**, 117.

## THE S.H.M.O. GRADE

The Ministry of Health has now issued its scheme for reviewing the grading of senior hospital medical officers.[1] The so-called review does not constitute an appeal for S.H.M.O.s dissatisfied with their initial grading. It is a fresh assessment of their status, and its purpose is to pick out S.H.M.O.s who have, "as a result of further experience since their grading, achieved consultant status." S.H.M.O.s in consultant appointments who are graded as consultants by the new review committees will be eligible for consultant pay, but those now in S.H.M.O. posts, even though graded as consultants by the committees, will not obtain consultant pay in their present posts. They must apply for consultant posts, and only on appointment to them can they receive consultant pay. The Joint Committee representing consultants and other hospital medical practitioners has had to accept this decision, for the need for some S.H.M.O. posts in a limited field has been agreed by the Joint Committee. But no doubt regrading as a consultant will help the man who wants to apply for a consultant appointment. A welcome feature of the new scheme is that it will include in the review junior hospital medical officers and general practitioners remunerated under paragraph 10(*b*) of the Terms of Service.

The review committees are to be composed of four members appointed by regional hospital boards—one physician, one surgeon, one obstetrician, and one consultant in the branch concerned—and three members nominated by the appropriate Royal College—one physician, one surgeon, and one consultant in the branch concerned. An important new proviso concerns the grading of a medical officer of health who holds a hospital post as S.H.M.O. in infectious diseases. In such a case two consultants in infectious diseases must be included in the review committee—one selected by the board and one nominated by the Royal College of Physicians. In allowing the Royal Colleges to nominate three members of a review committee, the Ministry has gone some way towards meeting the Joint Committee's request that the committee itself should nominate these members. Since the Joint Committee in part represents the Royal Colleges, there is unlikely to be any serious conflict of opinion on these nominations.

A disappointing feature of the Ministry's scheme is that any changes in grade, and therefore in pay, made by the review committees will not be retrospective but are to take effect from January 1, 1952. The decision is in accordance with the view that this is a reassessment and that the original gradings were regarded as definitive at the time they were made. A number of doctors understandably felt aggrieved by their earlier treatment, though the B.M.A. was active in getting some unjust decisions altered. Not all the first decisions were wise ones, partly because they had to be founded on imponderable features of professional life. It is to be hoped that the new review will give greater satisfaction. If past errors are not to be repaired, here at least is an opportunity for preventing injustice from rankling for years to come in the hospital service.

[1] See *Supplement*, p. 21.

## THE HEALTH OF IRELAND

The last five years have seen large changes in public health administration in the Republic of Ireland. In 1947 a Department of State was created to be concerned entirely with the administration of health services. A Health Act, a Mental Treatment Act, and an Act placing health services on a new financial basis have been passed, and these, together with a Public Assistance Act of an earlier date, have laid the foundation for a greatly improved health service for the community. The Department of Health has recently issued its first report,[1] which covers the period 1945 to 1949. It follows the plan of the annual reports of the English Ministry, with its chapters on administration and legislation, on each of the important health services, on hospitals, and on the ancillary work which falls to the public health medical officer.

The Irish birth rate during the five years under review fluctuated between 22.0 and 23.2 per thousand. The death rate fell to 12.1 in 1948; this compares with 11.0 for England and Wales in that year and 11.2 for Northern Ireland. Infant and maternal mortality and mortality attending the common infections have been reduced. More than a half of those who die between the ages of 25 and 35 die from tuberculosis in one form or another. Though tuberculosis mortality has decreased since the turn of the century from 2.53 to 1.04 per thousand, it is still double the rate for England and Wales. The report states that the facilities for preventive and curative treatment now are better than they were five years ago, and are showing improved results already. The mind of the public has been directed by health propaganda and by financial inducements to seek early diagnosis and treatment. The building of three regional sanatoria—in Dublin, Cork, and Galway—is a principal item in the anti-tuberculosis campaign. Illustrations of the Dublin building appear in the report, and it is evidently a big project.

Ireland is going ahead with its hospitals. It is hoped to complete by 1955 a short-term programme providing some 7,000 additional beds. Of the beds in Irish hospitals, numbering some 44,000, about three-fourths are under the local authorities. The public assistance medical service has some distinctive features. It provides free medical treatment for poor persons. For this purpose the country is divided into 589 dispensary districts, staffed by 646 medical officers and 694 midwives. The service is backed by the district and county hospitals, and the dispensary doctors may obtain the services of a consultant for any patient under their care. The cost of the expanding health services in Ireland is to be shared equally between the State and the local authorities. The total cost in 1948–9 was over £6.5m., and of this the tuberculosis services accounted for nearly £1m.

---

Sir Cecil Wakeley was re-elected President of the Royal College of Surgeons of England on July 12. He was first elected President of the College in 1949.

[1] *First Report of the Department of Health*, 1945–1949, obtainable from the Stationery Office, Dublin, price 2s. 6d.

## *REFRESHER COURSE FOR GENERAL PRACTITIONERS*

# INFERTILITY

BY

**T. N. A. JEFFCOATE, M.D., F.R.C.S.Ed., F.R.C.O.G.**

*Professor of Obstetrics and Gynaecology, the University of Liverpool*

"The Divinity which presides over maternity is Chance."
—BALZAC.

The unhappiness, marital problems, and even ill-health which can result from childlessness require no emphasis. Approximately 8% of marriages in this country are involuntarily sterile, and in another 10 to 11% the couple succeed in having only one or two children, despite unrestricted efforts to have more. Fertility and infertility are relative rather than absolute states, comparatively few individuals being either completely sterile or fully fertile. Provided there is no absolute bar to conception on either side, the fertility of a marriage is the sum of the fertilities of the two partners. Low fertility on one side can to some extent be countered by high fertility on the other, but low fertility in both partners may result in a failure to conceive.

There is always a cause for infertility, and the frequency with which this is found depends on the thoroughness of the search. In many cases, however, several adverse factors are operative, and if these are distributed between the partners it may be impossible, even if it were desirable, to apportion the blame. The main fault is found in the female more often than in the male, but in any series of infertile marriages 40% of the husbands can be shown to be subfertile.

It is unreasonable to subject the wife to complicated tests and treatment without assaying the husband's fertility, but it is equally unreasonable to proceed to treat male infertility without first making certain that there is no bar to conception on the female side.

### When Should Sterility be Investigated?

A highly fertile couple practising coitus regularly take an average of six to seven months to achieve a pregnancy, and four out of five women conceive within one year of marriage provided they do not practise contraception. In younger couples it is usual to demand evidence of two years' infertility before embarking on its serious investigation, but there is much to be said for not waiting longer than one year, especially if the woman is over 30 or the man over 40. Indeed, a full clinical examination of both partners, and possibly semen analysis, is indicated as soon as any couple become worried.

### Assessment of Male Fertility

Paternity is probably the best proof of male fertility, yet it can be misleading; the incidence of subfertility, as judged by semen analysis, is as high among men who have been responsible for one pregnancy only as among those who have never impregnated any woman. Men who have induced two or more pregnancies usually have good-quality semen, although even in these the effect of advancing years or of intercurrent disease must be excluded. There are, therefore, very few cases of infertile marriage in which investigation of the male partner is not essential. A careful inquiry into past illnesses and an examination of the genitalia will reveal some finding of note in about 50% of subfertile men. In others it is disclosed only by semen analysis. The demonstration of spermatozoa in the vagina or cervix after coitus is inadequate for this purpose, and condom specimens are also unsatisfactory.

The specimen should be collected by interrupted coitus or by masturbation into a dry and clean glass container, after two or three days' continence. It should be kept at atmospheric temperature and should reach a pathologist experienced in seminology as soon as possible, though a delay of six hours is not incompatible with obtaining useful information. At least two separate tests are desirable, and any one specimen is assessed by weighing one character against another. For example, a low percentage of morphological abnormalities may compensate for a poor sperm count. A small volume detracts from a high sperm density. A very high volume with resulting dilution can be a disadvantage. Caution is necessary in assessing the significance of motility of spermatozoa, because it varies so much with the conditions of the collection and storage of the specimen. When the number and morphology of spermatozoa are good, the finding of poor motility can generally be disregarded as being due to an error in technique. The following table should be accepted only as a rough guide, and should be interpreted on the lines indicated above.

| | Good Fertility | Moderate Fertility | Low Fertility | Very Low Fertility |
|---|---|---|---|---|
| Volume of fluid .. | 2 to 5 ml. | 1 to 2 ml. | 0·5 to 1 ml. | Less than 0·5 ml. |
| No. of sperm per ml. | Over 60 million | Over 30 million | Less than 30 million | Less than 10 million |
| Motility at 6 hours | 80% | Over 50% | Less than 50% | Less than 50% |
| Normal morphology (head, body, and tail) | 80% | 50% | Less than 50% | Less than 50% |

The practical importance of chemical analysis of seminal fluid, except possibly in regard to fructose, which reflects seminal vesicle activity, is not yet clear.

In cases of azoospermia and oligospermia, another step in the investigation is testicular biopsy, which is a simple procedure carried out under local analgesia. It makes it possible to distinguish between azoospermia due to faulty spermatogenesis and that due to a mechanical obstruction in the vas or epididymis.

The finding of low fertility on the husband's side should be understated to the couple concerned, partly because knowledge of male sterility may disturb marital harmony, but mainly because it is by no means uncommon for men with extremely low sperm counts to be responsible for an occasional pregnancy. It should never be said that pregnancy is *impossible*, even if no spermatozoa can be found.

### Disorders of Coitus

The frequency of coitus and any difficulties associated with it deserve special inquiry. Male impotence is more common than is generally recognized, and "partial

impotence," a condition in which there is erection and penetration without emission, can be difficult to exclude. Women married for several years may be found virginal either because of ignorance, vaginismus, or male impotence. Some patients are unaware that the fertile period is between the 8th and 18th days of a 28-day cycle and that coitus should be practised every 48 hours at that time to provide the optimum chance of pregnancy. Overindulgence, unless carried to extremes, does not significantly lower fertility, and there is no unequivocal evidence to show that periods of continence improve the prospects. The escape of semen from the vagina after coitus is normal, and women who think that their barrenness is due to effluvium seminalis can be reassured on this point. Failure of the woman to achieve orgasm is also not a bar to conception.

### Tubal Disease and Tubal-patency Tests

Partial or complete tubal occlusion is nearly always the result of previous peritonitis or salpingitis, though there is not always a definite history of such an illness.

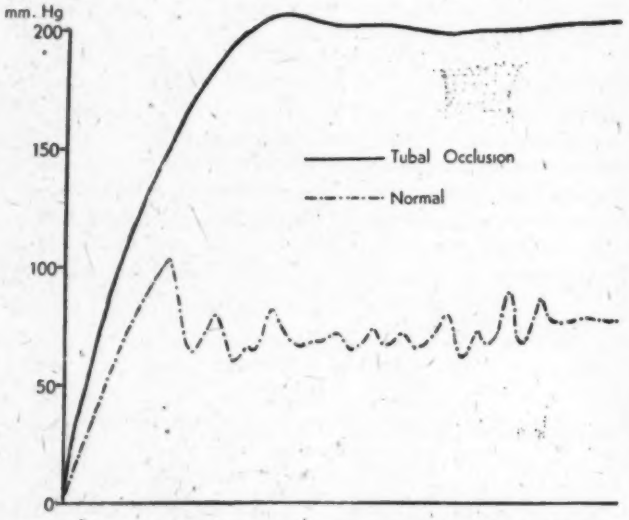



FIG. 1.—Kymograph records indicating (1) bilateral tubal obstruction—the pressure is not allowed to rise above 200 mm. Hg, because this is the limit of safety; and (2) normal tubal patency—gas passes through freely at a pressure of 70 to 100 mm. Hg.

Tubal-patency tests are best carried out during the two weeks following the conclusion of a menstrual period, and can be done with or without anaesthesia, but the results require the most careful interpretation.

*Insufflation.*—Air or carbon dioxide is injected through the cervix, and patency of the tubes is assessed from the pressure changes in the system, which are noted on a simple manometer or recorded by a kymograph (Fig. 1). Failure to pass gas into the peritoneal cavity suggests that both tubes are obstructed, but it is wrong to reach this conclusion on a single negative test, for this can be accounted for by muscle spasm at the utero-tubal junctions. A positive test ordinarily means that at least one tube is open, but can also be deceptive in that it may be obtained in cases of hydrosalpinx and of peritubal adhesions.

*Hysterosalpingography.*—A non-irritant radio-opaque medium is injected through the cervix, and its flow through the uterus and tubes is followed by *x*-ray screening and filming. A further radiograph is taken 24 hours later in order to study the dissemination of the medium

FIG. 2.—Hysterosalpingograph showing apparently normal tubes.

FIG. 3.—Radiograph taken 24 hours after Fig. 1. The radio-opaque medium has passed through the tubes, but it is pocketing in the peritoneal cavity. This suggests the presence of pelvic adhesions.

FIG. 4.—The 24-hour radiograph of a hysterosalpingography series obtained some months later from the same patient as in Figs. 1 and 2 after operation for separation of peritubal adhesions. The medium now spreads freely.

through the peritoneal cavity. Again the proper interpretation of the findings requires experience and care; a hold-up at the utero-tubal junctions is often due to spasm alone. Even when the tubes are open there may be intrapelvic adhesions which interfere with the passage of the ovum from ovary to tube—a cause of sterility which is often overlooked and, moreover, one which is amenable to treatment. It can be recognized by pocketing of the radio-opaque medium (see Figs. 2, 3, and 4).

Each of the above tests has its place, but the investigation of a case of infertility can never be said to be complete unless hysterosalpingography has been performed. Although primarily used for diagnosis, tubal-patency tests have, for reasons still uncertain, some therapeutic value, as is shown by the fact that conception sometimes occurs within the following three months.

### Dilatation and Curettage

Dilatation of the cervix is also useful in treatment of nulliparae, probably because it allows better drainage and prevents inspissation of the cervical plug. Curettage is mainly for diagnosis, and its objects are: (1) to determine the occurrence of ovulation by demonstrating secretory changes in the endometrium during the second half of the menstrual cycle; and (2) to exclude tuberculosis or other disease of the endometrium. Tuberculous endometritis is found in 2 to 5% of women who seek advice on account of infertility, and they may have no other symptoms. A single negative biopsy does not exclude genital tuberculosis, nor indeed does a positive tubal-patency test, because the tubes remain open in 50% of cases.

### Time and Frequency of Ovulation

Female sterility may be caused by a failure to ovulate. Sometimes associated amenorrhoea and genital hypoplasia give a clear guide to the ovarian trouble, but a normal menstrual cycle does not necessarily denote regular ovulation. Anovular menstruation occurs occasionally in nearly all women, but few make a habit of it, and it probably accounts for not more than 5% of the cases of sterility.

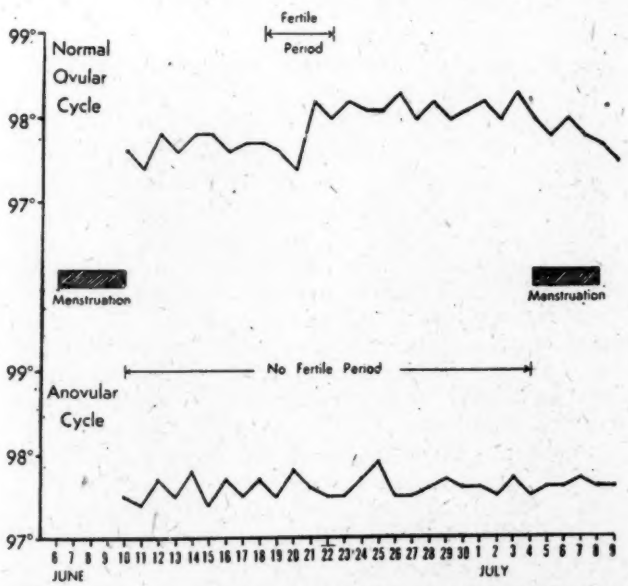



FIG. 5.—Daily temperature records likely to be obtained in an ovular cycle and an anovular cycle. The change from low to high level in the former marks the occurrence of ovulation.

Failure to ovulate may be demonstrated by premenstrual or menstrual endometrial biopsy, but this and other rather complicated investigations, unless repeated, give information concerning one cycle only. A daily temperature record is a more simple and convenient, although rough, method for studying the ovulation function during several months. The woman is instructed to take her oral temperature (rectal or vaginal records are unnecessary) on waking each morning, and to chart it. Ovulatory cycles are biphasic, the temperature tending to be about 0.8° F. (0.4° C.) lower in the first than in the second half of the cycle. Ovulation occurs just before or at the time of the sudden change from low to high level (see Fig. 5).

The advantage of a temperature chart is that it shows the approximate time as well as the occurrence of ovulation, and therefore the time when coitus is most likely to be fruitful. Its disadvantage is that it is a daily reminder of childlessness, and it tends to make couples time their acts of intercourse with mathematical precision. If temperature recording becomes necessary it should never be continued for longer than three to four months, by which time it should be possible to assess the ovulation habit.

### Post-coital Tests

An abnormality in the physical or chemical properties of the mucus plug in the cervix which makes the mucus impervious or injurious to spermatozoa is a theoretical cause of infertility. Tests for cervical hostility include the examination of mucus for active spermatozoa at intervals after coitus, and the removal of mucus to see how normal spermatozoa from a fertile donor react to it *in vitro*.

Enthusiastic claims are made for these tests and, when cervical hostility is demonstrated, for its correction by hormones, antibiotics, and other remedies. Yet equally good and even better results for the treatment of infertility are obtained in clinics where post-coital tests are never carried out, and where cervical hostility, other than that which might result from obvious cervical disease or that which might be corrected by dilatation, is regarded as insignificant. Until more evidence is available the place for and the interpretation of post-coital tests remain *sub judice*.

### Treatment of Sterility

The object of treatment is to eliminate so far as is possible any infertility factors found in both husband and wife. Obvious disease in their genital tracts should be treated according to its nature. Both should be considered together, for when the fertility of one cannot be improved it may be cancelled out by raising the fertility of the other. For example, poor spermatogenesis in the husband might be counteracted to some extent by dilating the cervix or correcting a retroversion in the wife.

#### Male Infertility

When azoospermia is due to obstruction in the epididymis or vas, short-circuit operations carried out by those with special experience are not infrequently successful. Impotence, too, can often be cured by a psychiatric approach, but it is rarely benefited by androgens unless it is clearly caused by testicular underactivity,

in which case there is usually defective spermatogenesis as well. It must be remembered that potency does not confer fertility.

The treatment of faulty spermatogenesis is not very satisfactory, and attention to general health and mode of existence offers the best hope. Follicle-stimulating hormone, 500 to 1,000 i.u. intramuscularly twice weekly, or thyroid, 1 gr. (65 mg.) at night, for two to three months, may help and can do no harm. Vitamin E, although often prescribed, is useless so far as restoration of testicular function is concerned.

### Female Infertility

*Dilatation of the Cervix, Tubal Insufflation, Hysterosalpingography.*—These procedures, although primarily diagnostic, have a definite therapeutic value, and it is therefore sometimes justifiable to repeat them at intervals. However, organic obstruction in the tubes cannot safely be overcome by these means.

*Vitamin E.*—Despite its widespread use in the past, there is no evidence that this ever improves the chances of conception.

*Hormone Therapy.*—The empirical use of hormones is to be deprecated, because not only is it without merit but it may disturb an essentially normal ovario-uterine cycle and reduce rather than improve the chances of conception. The only clear indication is a proved failure to ovulate, when the appropriate treatment is either with gonadotrophin or with oestrogen and progesterone administered cyclically. Some give oestrogens in the first half of the cycle to overcome uterine hypoplasia or to make cervical mucus more receptive; others give progesterone or ethisterone premenstrually to prevent a hypothetical early abortion. None of these conditions is a proved cause of sterility, and there is good reason to doubt whether such treatments do any more than give the patient hope.

*Radiation Therapy.*—Low-dosage "stimulative" *x*-ray treatment to the ovaries has a few enthusiastic supporters, but its rationale is uncertain and its value unproved. Moreover, it involves the theoretical dangers of permanent injury to the ovary and of the fertilization of a damaged ovum. Nevertheless, a higher incidence of malformed foetuses after this treatment has never been demonstrated.

*Correction of Uterine Position.*—Retroversion and retroflexion can usually be neglected as causes of infertility, but occasionally they appear significant. When other factors have been excluded and a woman remains childless correction of retroversion is worth while. This is usually done by means of a Hodge pessary, but occasionally some form of operation is justified.

*Pre-coital Douches.*—This is a simple and harmless but empirical form of treatment, worthy of a limited trial. A douche of 1% sodium bicarbonate given 10 to 15 minutes before coitus sometimes appears to help, possibly by softening the cervical plug. Alternatively, a douche which consists essentially of Ringer's solution with a glucose supplement* may give spermatozoa extra vitality, and may be indicated when the semen is faulty.

*Salpingostomy and Salpingolysis.*—When the Fallopian tubes are found closed the prognosis is poor but not hopeless, depending on the type of infection causing the obstruction. If this be tuberculous nothing useful can be done. If it be gonorrhoeal then again salpingostomy gives poor results, because the endosalpinx is usually permanently damaged. If, however, the tubes have been closed as a result of pelvic peritonitis—as in the case of appendix abscess, for example—operative treatment offers a good chance of cure. When the adhesions are separated in these cases the freed tube is often found to be essentially normal (see Figs. 2, 3, and 4). Again, if the inner end of the tube is obstructed but the outer part is healthy resection of the diseased portion and implantation of the remainder into the cornu of the uterus may be successful.

*Proprietary tablets, each one of which when dissolved in a pint (570 ml.) of water gives the required solution, are now on the market.

### Artificial Insemination

Even if it is ever in the interests of the patient, which is extremely doubtful, the ethical, religious, and legal objections to artificial insemination with donated semen are so strong that most authorities now take the view that it should never be employed as a way of circumventing male sterility.

Intracervical insemination, using the husband's semen, however, is sometimes indicated when there is disease or deformity of the cervix which makes it difficult for spermatozoa to enter. Intravaginal insemination can be employed when coitus is prevented by impotence or other condition, and the wife can usually be taught to carry it out herself at home. When the quality of semen is subnormal, however, artificial insemination probably offers no better chance of conception than does coitus.

### Results of Treating Infertility

No matter what treatment is applied or what advice is given, conception will follow in a certain number of cases—this is inevitable by the laws of chance which govern conception. It is all too easy to claim a coincidence as a dramatic cure, and this is the reason why so many treatments have their advocates. Scepticism in these matters is not popular, but it is justified by the findings in carefully documented series of cases. Of those women who consult a gynaecologist on account of sterility of two or more years' duration approximately 50% have at least one pregnancy within the next 15 years, and in not less than half of these the occurrence is entirely unrelated to treatment. Indeed, 3 to 4% conceive before there is time for any investigation or treatment. Moreover, the occurrence of a pregnancy after treatment does not necessarily mean that fertility is raised. As often as not the couple find it impossible to repeat the performance. It is therefore usually wise never to claim a "cure" for any form of treatment of sterility.

### Dangers of Investigating and Treating Sterility

With proper safeguards the minor operative procedures described above carry little risk to life, but acute salpingo-oophoritis follows within seven days of tubal-patency tests in 0.5 to 1% of cases. This is not because infection is introduced at the time of operation, but because the interference activates an unsuspected and dormant pre-existing disease. The most serious exacerbations occur in cases of pelvic tuberculosis.

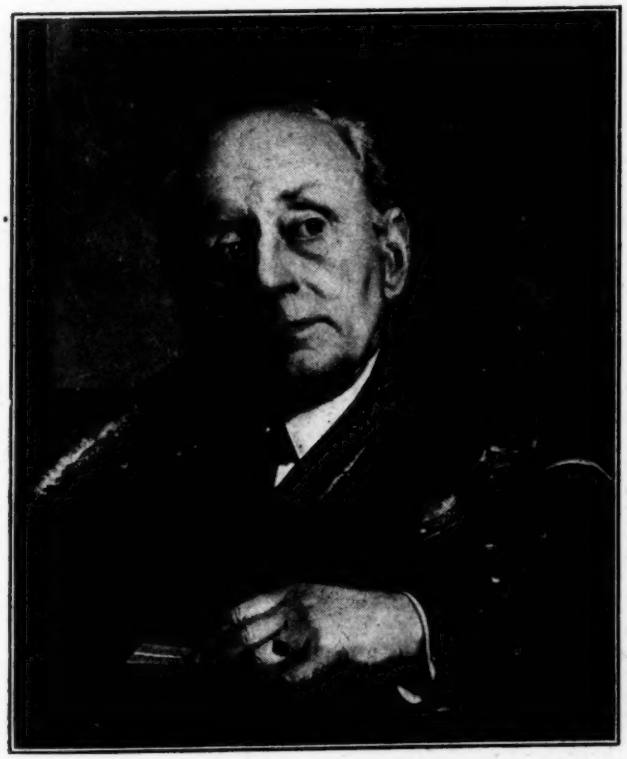
When pregnancy occurs in a subfertile woman its risks are greater than average: tubal pregnancy, abortion, toxaemia of pregnancy, difficult labour, stillbirth, and neonatal death are all more common. A higher incidence of foetal malformations is suggested but not proved. When, therefore, a pregnancy comes to a woman who has waited long its management demands the most rigorous attention.

The greatest danger of investigating and treating infertility, however, is that it may concentrate the patients' attention on their problem, and convert a complaint into an obsession. It can cause profound unhappiness and estrangement between the partners in marriage. Therefore investigations should never be unduly protracted or complicated. Clinical examination, semen analysis, tubal-patency tests, and endometrial biopsy, *if properly performed and interpreted,* will either be followed by pregnancy or reveal the causes of infertility in the great majority of cases. Treatment should be as rational as possible, and if not successful within a reasonable time should be abandoned. There is always an optimum time to call a halt, and one of the general practitioner's main duties may be to protect his patient from those whose enthusiasm clouds their sense of proportion.

In many cases the best service is rendered merely by giving the infertile couple a reasoned assessment of their chances of pregnancy, so that they may plan their lives accordingly. In this it is usually wise to be slightly more optimistic than is justified by the findings, and to avoid so far as possible saying anything which might lead to recriminations between man and wife. The question of adoption, if it arises, is one to be answered by each couple individually rather than by their medical attendant.

## PRESENTATION TO LORD MORAN

At a dinner held at the Royal College of Physicians on July 10 Lord Moran was presented with the portrait here reproduced. Mr. Winston Churchill, who was recently elected an honorary Fellow of the College, made the presentation. Lord Moran was President of the Royal College of Physicians from 1941 to 1950, and to give some token of appreciation of his long and valuable service in that office the Fellows of the College formed a subscription fund in order that his portrait might be commissioned. The artist chosen was Pietro Annigoni, the Florentine painter. After thanking the Fellows for their gift and for their kindly feeling towards him, Lord Moran spoke of the place of the College in the history of medicine and of the nation. "From 1518 to 1858 (the year of the first Medical Act) the College governed medicine and the presidents governed the College." Remarking that many of the presidents seemed to have enjoyed the friendship of their monarch or his first Minister, Lord Moran said that it should not be forgotten how great a part the profession had played in the building of the nation, though, unlike the Church and the Law, it had no place in the official hierarchy. Nevertheless, he could say deliberately that in the 40 years in which he had known the profession it had done more for the well-being and contentment of the people than the rest of the community put together.



## BRITISH EMPIRE CANCER CAMPAIGN

The 28th annual meeting of the British Empire Cancer Campaign was held at the House of Lords on July 10, Lord Horder presiding. A message was read from the Duke of Gloucester, president of the Campaign, in which he said that it was encouraging to learn that there had obviously been no slackening of the pace of research; on the contrary, the intention to intensify their efforts, which was declared soon after the war, was being conscientiously fulfilled.

Lord HORDER said that the cancer problem was sometimes likened to a jigsaw puzzle in which the pieces were slowly fitted together to form a complete picture. A better simile might be Theseus groping his way into the labyrinth to slay the Minotaur lurking in its depths, and leaving behind him as he ventured a coloured thread to enable him to find his way out again. Research workers were slowly penetrating this maze, and the thread which they were leaving behind them was their writings in the many scientific journals of the world. It was inevitable that such a search should take them up many blind alleys—in other words, that they should conduct many experiments which led to nothing. But even this was worth while, as it was largely by a process of elimination that future workers could proceed with sureness.

Professor R. W. SCARFF, in presenting the annual report, on which he congratulated the honorary editor, Sir Heneage Ogilvie, said that there was nothing in it which was sensational and little that was dramatic, but it represented a year's solid achievement in the advance of knowledge of cancer. The scientific publications numbered over 200, and were to be found in many journals devoted to different aspects of medicine. The work was conducted on two main lines: the prosecution of fundamental research into the cause of cancer, and the application of the knowledge already gained to the recognition and treatment of the individual case. Disappointments were inevitable in cancer work, and lines of research which at first might appear promising had to be given up because they led nowhere. He mentioned as an example the recent discovery that mammalian tumour tissue was capable of producing further tumours even after being completely dried and submitted to a temperature of −79° C., which was taken as clear-cut evidence of the presence of an infective agent; but it had been found that the tumours were simply the effect of cell transmission and gave no support to the theory of infection. Under the second heading—i.e., the application of knowledge already gained—a number of investigations and observations bearing on the treatment of patients with cancer were included in the annual report. Assistance in the accurate recognition and diagnosis of tumours was given by the histological panel set up under the Campaign in co-operation with the Pathological Society of Great Britain and Ireland.

Many people, said Professor Scarff, supposed that the big advances made in medicine had been the result of happy accidents. This was not so; they were due rather to the falling of seed into ground already suitable and adequately prepared. It was only when the knowledge of the subject had attained a sufficient breadth that a spectacular advance was possible. It was becoming increasingly evident that cancer did not present a single problem, but that many different forms of the disease had different modes of origin and gave a different response to alterations in environment.

Mr. P. J. F. CHAPMAN-WALKER, dealing with the financial side of the Campaign, mentioned that in these days of heavy taxation they could no longer rely on large individual subscriptions. Gifts of £500 or more accounted for one-third of their income a quarter of a century ago, but now they accounted for only one-twentieth.

The Nuffield trophy for the most outstanding efforts during the year to raise funds for the work was presented to the representatives of Boston in Lincolnshire.

# Reports of Societies

## INTERNATIONAL SOCIETY OF ORTHOPAEDIC SURGERY AND TRAUMATOLOGY

In its twenty-first year, the Société Internationale de Chirurgie Orthopédique et de Traumatologie (SICOT) held its fourth meeting, from May 21 to 25, in Stockholm.

### Low Back Pain and Sciatica

In a symposium opened by Dr. J. S. BARR (U.S.A.) special attention was paid to the results of surgical treatment of protruded intervertebral disks. It appeared that with careful selection of cases and good technique sciatic pain ascribed to protrusion of an intervertebral disk should be relieved in about 90% of patients submitted to operation, failures being due to diagnostic errors, neurosis, too long delay, multiple disk protrusion, insufficient removal of disk substance, and to post-operative adhesions caused in some cases at least by infection. In the absence of root pain, the results of disk removal were less satisfactory and there was a case for simultaneous arthrodesis. A recent swing back towards myelography was supported by Dr. Barr and illustrated by papers by Dr. FOLKE KNUTSSON (Sweden) on lumbar myelography with water-soluble medium and Dr. J. J. HERBERT (France) on epidural myelography. Drs. KNUT LINDBLON (Sweden) and PH. ERLACHER (Austria) referred to nucleography, made possible by the injection of an opaque medium into the suspected nucleus pulposus—a procedure that had not yet been known to lead to protrusion, but nevertheless was more suitable for research than routine use. Some Swedish investigations into the structure, physiology, and pathology of the intervertebral disks were quite outstanding. Dr. KARL HIRSCH showed that degenerative changes, without histological manifestation of repair, were common at all ages, habitually proceeding from the annulus outwards. Distension of the degenerated disk with liquid would excite the patient's usual pain. Dr. BENGT SYLVEN described the minute structure of the nucleus pulposus with its chondrocyte-like cells lying in a matrix of interlacing collagen fibrils coated with a polysaccharide-protein complex which rendered them hydrophilic and which diminished with age. Dr. STEN PAULSSON and Dr. OLLE SNELLMAN had found diffusion in this material slow; the nutrition of the nucleus remained a puzzle.

### Vitamins and the Skeleton

Dr. RAFFAELE ZANOLI (Italy) summarized our knowledge of the influence of vitamins upon the skeleton. Dr. F. KODICEK (Great Britain), with others at the Strangeways Research Laboratories, Cambridge, had studied the effect of chronic partial deficiency of vitamin C in a large number of guinea-pigs. Besides the dental changes, osteoporosis and failure to convert pre-collagen into collagen, characteristic of acute scurvy, hyperostoses and arthritic changes also were found in chronic scurvy. Experimental fractures of the fibulae healed slowly without proper callus formation, and hyperostotic tissue developed about the site of injury and sometimes in the opposite limb. The joint changes resembled human rheumatoid arthritis histologically and were sometimes relieved by cortisone acetate. Alkaline phosphatase, which is ordinarily found in a recent wound a few days after injury when collagen formation is at its peak, was absent from the wounds in vitamin-C deficiency; the collagen fibres were irregularly arranged and ensheathed in a mucopolysaccharide, a manifestation of the influence of vitamin C on mucopolysaccharide metabolism. Dr. M. CASUCCIO, with Dr. G. BANTHO (Italy), had found that vitamin-E deficiency delayed callus repair of experimental fractures.

### Congenital Dislocation of the Hip

Dr. E. SEVERIN (Sweden) had studied the development of the hip after closed reduction, and had observed that the soft tissue almost always interposed between the head and the acetabulum gradually atrophied if the head remained in place. Consequently, interposition did not justify operation, which should be reserved for the few cases in which closed reduction failed. After reduction, the chief cause of failure, Dr. E. PLATEAU (Norway) believed, was cervical anteversion, which, if greater than 45 degrees, called for high rotation osteotomy, with plating, as part of the primary treatment. The tendency to allow the child as much freedom of movement as is consistent with control of the hips was illustrated in a metallic retention apparatus described by Dr. ANDRÉ TRÈVES (France). Dr. JEAN JUDET (France) had treated forty cases of old unreduced dislocation by replacement of the femoral head by an acrylic substitute and placing it in a deepened or, if necessary, new acetabulum.

### Chemotherapy of Tuberculosis

Dr. P. GÉRARD-MARCHANT (France), Drs. SVANTE ORELL, MAC FELLÄNDER, and OLOV LINDAHL (Sweden), and Professor AKIF CHAKAR (Turkey) had confirmed that streptomycin improved the results and increased the safety of surgical treatment, and possibly allowed it to be undertaken earlier; but conservative orthopaedic treatment was considered still important.

### Other Subjects

Other papers included an account by Dr. P. K. DURAISWAMI (Great Britain) of the production of seemingly heritable congenital abnormalities in the chick by injection of insulin into the yoke, the work of Professor J. TRUETA (Great Britain) on the stimulation of growth of long bones by obliteration of the nutrient vessels, and a preliminary report by Dr. SVEN KIAER (Denmark) on hip arthroplasty with an acrylic head carried out for various conditions in fifty patients. In arthroplasty by Judet's method it seemed to matter little whether the capsule was excised or retained and sutured. Pain was relieved or greatly improved in nearly all the patients. Dr. HAROLD B. BOYD (U.S.A.) had devised a method of determining the viability of the head of the femur, after fracture of its neck, by injecting $P^{32}$ into the blood stream and then comparing the readings obtained in the head of the femur and in the trochanteric region with a sterilizable Geiger counter.

The meetings took place in the Great Concert Hall, whither successive Nobel prizemen have come to receive their prizes. Not only did Swedish hospitality surpass itself, but the lovely city of Stockholm was at its best in a cloudless spring. Swedish organization proved as efficient as its

hospitality was warm ; there were such pleasures as a soirée in the National Museum and a reception at the famous modern Town Hall, followed by a trip by water to the Palace of Drotningholm and a performance of music and ballet in the eighteenth-century State Theatre there. The labours of the Congress were crowned with a banquet.

At a general meeting it was reported that Bulgaria, Egypt, Israel, Luxembourg, Mexico, and New Zealand had joined the Society and it was agreed to readmit the German members. Professor Sir Harry Platt was re-elected President. It is proposed to hold the 1954 meeting in Switzerland.

## FESTIVAL SYMPOSIUM ON ODONTOLOGY

On July 9 a symposium on "Odontology" was held at 1, Wimpole Street, London, W.1. This was the 25th of the Festival Scientific Meetings sponsored jointly by the British Medical Association and the Royal Society of Medicine. Sir WILLIAM KELSEY FRY was in the chair.

Dr. A. H. DOUTHWAITE reviewed the change of outlook of the physician on dental sepsis over the last 25 years. A quarter of a century ago sciatica, rheumatoid arthritis, fibrositis, and similar diseases, the aetiology of which was not clearly understood, were said to be due to focal sepsis in the jaws, sinuses, or alimentary tract. He thought that to-day there was a saner outlook on the matter.

### Medical Sequelae of Dental Sepsis

Dental sepsis could spread in two ways, either locally or distantly via the blood stream. Among the lesions which could be considered attributable to local spread from open dental sepsis were acute and chronic glossitis, recurrent sore throat, acute parotitis in debilitated patients, enlarged lymphatic glands of the cervical chain, and chronic gastritis. In considering the lesions which might follow haematogenous spread from dental sepsis, Dr. Douthwaite said that the cardiovascular system was the most vulnerable. Extraction of teeth could give rise to a transient bacteriaemia, and in patients with congenital or chronic cardiac lesions a bacterial endocarditis might ensue. Chronic hypochromic anaemia could be caused by closed dental sepsis, which might be cured by removal of the offending teeth. Sudden thrombophlebitis in otherwise healthy veins could be attributed to focal sepsis. A purpura manifested in the lower limbs might follow dental extraction ; the platelet count was not altered and fragility tests showed no abnormality. The condition, which was possibly due to a transient toxaemia, cleared spontaneously. It was improbable that the digestive and genito-urinary systems were affected by haematogenous spread from infected foci in the jaws. In 25 years the speaker had noted five cases of pyrexia of unknown origin which he considered were due to dental sepsis.

In discussing the effect of focal sepsis in arthritic and rheumatic conditions, Dr. Douthwaite could find no sound scientific background for any relationship of the one to the other. The discovery of sulphonamides and antibiotics had been the final blow to focal sepsis in this connexion, as the organisms said to be responsible were sensitive to the antibiotics, yet their administration gave no relief.

### Sinusitis of Dental Origin

Mr. C. GILL CARY discussed the significance of dental sepsis to the E.N.T. surgeon under three headings: (1) Dental sepsis and disease of the pharynx and larynx ; (2) sinusitis of dental origin ; and (3) facial pain of dental origin.

Mass dental extractions as a pre-operative necessity were now a procedure of a bygone era. Nowadays only the removal of obvious dental sepsis was indicated, and the introduction of chemotherapy had reduced the risk of infection by oral organisms, as complications to pharyngeal and laryngeal operations, to a negligible factor.

Discussing sinusitis of dental origin, the speaker reported that, in a recent survey of 500 cases of maxillary sinusitis, 27 cases had been directly attributable to dental sepsis or to a dental operation. He remarked upon the chronicity of the sinusitis, the occasional difficulty in establishing the aetiology, and the excellent response to simple treatment if an early diagnosis was made. With regard to facial pain, the speaker discussed the differential diagnosis between dental pain and pain of a similar distribution secondary to disease of the nose and throat.

### Eyes and Teeth

Mr. J. H. DOGGART, speaking as an ophthalmologist, began with a brief reminder of the strong views held by ophthalmologists in the past who believed dental sepsis to be responsible for many ophthalmological ailments, including iridocyclitis, choroidal sclerosis, and retrobulbar neuritis. The outlook to-day was, however, much more reasonable. Direct spread of infection from the teeth and jaws to the eyes could occur, and he cited cases as examples. Focal sepsis in the jaws was not, in his opinion, often responsible for conjunctivitis or other inflammatory processes of the eyes or their adnexa.

### Plurifactor Dermatitis

Dr. W. J. O'DONOVAN discussed changes in the basic concepts of dermatology. Most practising dermatologists had been brought up to regard rashes, eruptions, infiltrations, and ulcers of the skin as "self-existing identities." Great importance was attached to their recognition, but little time was given to the study of their causes. To-day when reactions were observed to occur with fair consistency there was a growing tendency to describe these recognized types of disease as "pattern reactions." The idea of a single cause had long been in favour among medical men. It was well developed when Osler first clarified the clinical and pathological picture of ulcerative endocarditis. Nothing had been more striking than the rapid recognition in Spanish medicine that the rashes on the skin and mucous membranes of sailors from the Indies were to be attributed solely to a venereal sore that was the first site or focus of a later generalized infection.

Surgeons long ago had taught that amyloid disease of liver and spleen had its origin in an old, uncured osteomyelitis with a sequestrum, so that the notion that acute localized infections, especially in the nose and throat, might give rise to disease in other regions had readily and widely and for long been accepted. It had been accepted that bacteria causing focal infection might be discharged and conveyed by mechanical means so as to cause extension of the disease by reinoculation ; that bacteria might overcome local resistance and be conveyed to distant parts of the body by way of the lymphatics and the blood ; or, thirdly, that the micro-organisms might remain enclosed at the seat of focal infection from which their toxins were slowly and continuously absorbed. This idea was earnestly canvassed in the dermatological schools. Scarlet fever was reasonably attributed to a primary focus of infection in the tonsils. A most characteristic skin eruption, erythema multiforme, might be taken as a *locus classicus* of the use of this working hypothesis. The disease was attributed in standard textbooks of about 1927 to seven causes, of which one was "focal sepsis—e.g., of the teeth, tonsils, sinuses, etc." To-day, if the more modern editions of the same textbooks were consulted, it would be found that focal sepsis had been quietly dropped as a cause of erythema multiforme. Another disease which was no longer associated with a primary focus of infection, as once it had been, was lupus erythematosus.

To-day focal sepsis was not included in the indices of the latest textbooks. What was the explanation of this ? Dr. O'Donovan suggested that it would be found in a form of words more common in the United States than here, namely, "plurifactor dermatitis." A cause of a skin trouble did not produce manifest disease unless there was a previous

predisposition which might be due to a hereditary tendency of genetic origin or to sensitization at some time. The exciting cause might be a hurt to which the skin would have been unresponsive if the patient's reaction balance had not been upset by mental tension, shock, or a transient virus illness or a common cold. Many patients had focal sepsis, but few exhibited recognizable efflorescences.

### Oral Hygiene and Anaesthesia

The discussion which followed was opened by Dr. E. W. FISH, who said he was pleased to hear the unanimity of the speakers on the subject of focal sepsis. He reminded the meeting of the danger of dental extractions in heart disease, citing examples. He laid much emphasis on the point that eradication of apical infections did not necessarily render a mouth free from sepsis. The gingival and paradontal tissues could harbour sepsis, which on mastication might result in a transient toxaemia or bacteriaemia. He made a plea to the dental surgeons that when asked to eradicate focal sepsis they should make quite sure that no infection remained in the gingival and paradontal tissues.

Professor M. A. RUSHTON agreed with the assessment of dental sepsis which had been given. Two aspects of current practice, however, did not accord with present knowledge. There was inadequate provision in hospitals for the oral hygiene of patients who were to receive general anaesthetics. And, since the frequency and extent of bacteriaemia were closely related to the number of teeth extracted, the removal of very many teeth at one time from out-patients, as was still done in many dental practices, appeared most undesirable.

Several other speakers took part in the discussion.

## Preparations and Appliances

### OPERATION ARM-REST

Mr. DAVID F. THOMAS, F.R.C.S., orthopaedic surgeon, Scunthorpe Group of Hospitals and Lindsey County Council, writes: The most satisfactory position of the arms during operation should be that in which (1) the arms are held completely out of the way either of the surgeon or of an *x*-ray machine—for example, in internal fixation of fractures of the upper end of the femur; (2) there is no danger of traction palsy of the brachial plexus; and (3) the arms are accessible for injections or transfusions.

I have designed an operation arm-rest which, I think, fulfils these requirements. It consists of a metal base and two adjustable arm-rests. The arm-rests are screwed to the base, which is perforated by a series of holes to allow the distance between the arm-rests to be adjusted according to the size of the patient. Each arm-rest has a telescopic adjustment in both its vertical and its horizontal limb, and by means of this telescopic arrangement not only can the limbs be adjusted for length but the degree of pronation and supination can be altered (Fig. 1). The arms are held on the arm-rest by two simple slings—one on the horizontal portion which lies under the forearm in the region of the wrist, and one on the vertical portion which lies behind the lower part of the humerus. The slings are made not only with an adjustment for length but also with a button fastener to allow them to be undone quickly. The apparatus holds the arms in a position of rest, with adduction and flexion of the shoulder. It is a position which closely corresponds to that in which, when seated at a table, one rests the head in the hands with elbows on the table. As will be seen from Fig. 2 the arms are available to the anaesthetist for injections,

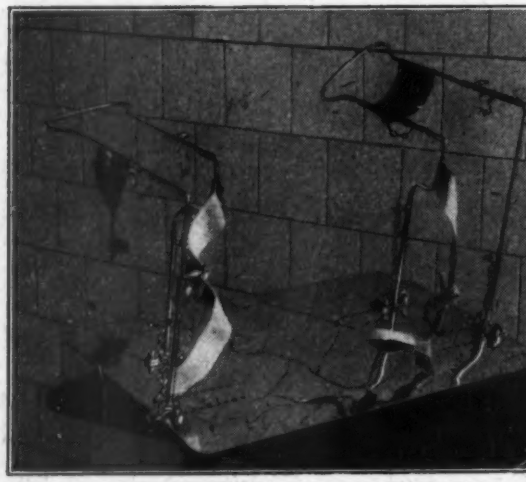


FIG. 1.—Showing especially the arrangement in the base for adjusting the distance between the arm-rests, and how the arm-rest can be tilted to alter the degree of pronation and supination of the forearm.

FIG. 2.—Showing the apparatus in place, as seen by the anaesthetist.

and the whole of the area of the arms and head can be sealed off from the operation field by a sterile towel.

This apparatus has been made for me by Messrs. Kempner, of Leeds, and I am grateful to Mr. Humphrey of that firm for his co-operation.

---

The Very Rev. Dr. John Flynn, for 40 years superintendent of the Australian Inland Mission, died on May 5 (*J. Amer. med. Ass.*, June 16, p. 669). Between 1912 and 1928 he established 13 small hospitals, each staffed by two trained nurses, and in May, 1928, introduced the first "flying doctor," who began his work in West Queensland. He covered an area larger than the whole of France. Two years earlier Alfred Traeger, an electrical engineer, had designed a small wireless set which received and transmitted both voice and Morse; the operator generated power for this by riding a fixed bicycle, the back wheel of which drove a generator, and a typewriter keyboard was designed which automatically sent out the message in code. While he pedalled the operator tapped out what he had to say; the normal range is about 500 miles, but the "transceiver" has been effective over 2,000. With the help of the flying-doctor medical chest in every homestead, many common illnesses can be treated, and emergency care can be given. The flying doctors are usually given other tasks by the Government; one of the first of them, Dr. Allen Vickers, was appointed a police magistrate, protector of aborigines, and mining warden. Once he saw twelve patients in one day, did two operations, held an inquest, conducted a court case, extracted many teeth, renewed five hotel licences, and issued permits for native labour. A dislocated shoulder was manipulated by instructions given by wireless, the doctor and patient being 400 miles apart. In 1940 McGill University recognized John Flynn's services by conferring on him the honour of doctor of divinity; seven years previously he received the O.B.E.

# Correspondence

## Psychiatry in General Practice

SIR,—During the last few weeks several articles on the psychoneuroses and their treatment have appeared in your columns, in the *Lancet*, and in the Cassel Hospital *Report*. Your issue of June 9 contains a very illuminating article by Drs. W. Sargant and E. Slater (p. 1315). Excellent though it is, I think it might have been improved, if I may say so, by a more realistic appraisal of the function of the G.P. Certainly, after reading this article many a G.P. will feel that the administration of E.C.T., the treatment of reactive depression, and so on is such a subtle affair as to compel him to seek the help of a psychiatrist at the very earliest moment. This is all very well, but as I see it the G.P.'s function is rather different. Surely, if so important a step as prefrontal leucotomy is to be considered, the G.P. would be well advised to collect some data which the psychiatrist will need before deciding upon an operation. He might, for instance, have an E.S.R. assessed to make certain that there is not a latent factor of toxaemia to be considered. Then he might well have a blood-sugar assessment, and preferably a blood-sugar curve made out, for I am sure these everyday factors have a place in such an important therapeutic decision. Perhaps the most important contribution a G.P. can make is to reveal factors in the patient's emotional environment that would not otherwise reach the psychiatrist. When the patient's escort is her mother highly important data may be suppressed. Furthermore, it is only the conscientious G.P. who is to be trusted to make a valid report on the patient's heredity.

Dr. W. L. Milligan (June 23, p. 1426) gives some convincing evidence of the value of his modification of the $CO_2$ abreactive technique. In my own mind I feel that such violent abreaction as he has elicited must have a very definite place in the psychiatrist's decision about further treatment by E.C.T., insulin, or psychotherapy, even though they "are not to be looked on as treatment for schizophrenia."

Dr. W. L. Neustatter's methods are very interesting. He apparently works to a time limit of three weeks. Under the National Health Service this is probably the best that can be done, but apart from such restrictions those of us who are still free in practice would demur at a time limit of this kind. All these writers refer to psychotherapy as if it could be compressed to fit in with the environmental situation, and that involves all the factors of environment, past treatment, and metabolic state of the patient. But Dr. Main's conclusion about psycho-analysis—i.e., "Could not always be offered when it was needed for the demands were more numerous than the hospital's facilities for this form of treatment"—brings us back to the same fundamental difficulty, to wit, the saving of psychiatric time. This is not a new discovery, but is one in which the official demand for rapid turnover of cases conflicts hopelessly with freedom and efficiency in all psychotherapeutic work.—I am, etc.,

Harrow-on-the-Hill. H. CRICHTON-MILLER.

## Poisoning by Home-perm Solutions

SIR,—The publication by Drs. W. A. Parker and J. R. Barr (June 16, p. 1363) of a case of poisoning by ingestion of "home-perm neutralizer" (potassium bromate solution) and subsequent correspondence from Dr. G. I. Benson (June 30, p. 1516) and Mr. K. Malcomson (July 7, p. 53) indicate that the accepted methods of dealing with this emergency are insufficiently known. These methods were published by Dr. R. M. B. MacKenna (*British Medical Journal*, 1950, **1**, 493, and *Lancet*, 1950, **1**, 424) and are as follows:

If the neutralizer has been swallowed, an emetic should be given (mustard water; zinc sulphate: apomorphine). Gastric lavage should be performed. One level teaspoonful of sodium thiosulphate (hypo) should be given in water after the patient has vomited. Demulcent drinks should follow. If shock arises, this should be treated, avoiding central nervous stimulants. Pain may be relieved by morphine. Intravenous administration of sodium thiosulphate has been employed, either by an injection of 10–50 ml. of a 10% solution or by an intravenous drip using 100–500 ml. of a 1% solution.

Drs. Parker and Barr suggest that the use of sodium thiosulphate is unnecessary and that nikethamide may be used.

Mr. Malcomson's letter calls for further comment. Potassium bromate in aqueous solution has a clear watery appearance. It is the thioglycollate "waving lotion" incorporating a "creaming" agent which looks milky. Owing to its strong smell and taste, accidental ingestion of waving lotion would be most unlikely; the point is noteworthy, since treatment of the patient in such a case would differ from that applied in a bromate poisoning case.

The artificial colouring of potassium bromate "neutralizer" solutions has been given careful thought, but has been avoided by at least one manufacturer on the grounds that it might tend to make the solutions more, rather than less, attractive to children. The detailed precautions already taken to emphasize the potentially dangerous nature of the neutralizer are considered to render the use of "home-perm" outfits no more dangerous in practice than the use of many common household chemicals such as ammonia, lysol, etc.—I am, etc.,

Gillette Industries, Ltd., Middlesex. GERALD OLLERENSHAW.

## Cortisone and Corneal Ulcers

SIR,—The paper by Drs. F. S. Lavery, L. E. Werner, D. O'Donoghue, P. M. Guinan, and J. Macdougald (June 9, p. 1285) reports a poor response to cortisone therapy in certain cases of corneal ulceration.

We are of the opinion that cortisone may be a dangerous agent in the treatment of corneal ulcers which involve the deeper layers of the stroma. Cortisone is known to exert a delaying action on new connective-tissue formation (Ragan, C., *et al.*, *Proc. Soc. exp. Biol., N.Y.*, 1949, **72**, 718). We have studied the effect of cortisone on the rate of corneal healing following thermal injuries in guinea-pigs, and have confirmed this delay in healing. Histologically we found a diminution in stromal regeneration at the site of the corneal lesion with resulting attenuation of the scar. It is conceivable that in deep corneal ulcers cortisone may increase the risk of perforation, and indeed one such case has already been reported by A. C. Woods (*Amer. J. Ophthal.*, 1950, **33**, 1325).—We are, etc.,

KENNETH C. WYBAR,
Glasgow FERGUS W. CAMPBELL.

## Syphilis in Different Races

SIR,—I was very interested in the letter from Dr. James Marshall, of Johannesburg (June 16, p. 1391). I entirely agree with his remarks about the annular skin lesions in early syphilis in the African native and with his statement that visceral lesions do occur not uncommonly, but I am sure he is mistaken in his opinion with regard to neurosyphilis. He criticizes the textbook view that neurosyphilis is rare in certain races, such as the North Africans. I spent some years before the war in the Anglo-Egyptian Sudan and made a study of the lesions of syphilis in many parts of that large sector of Africa. The manifestations varied considerably in different areas and in different races, but nowhere was I able to find any evidence of true neurosyphilis—that is to say, general paresis or tabes dorsalis—in a true native of the country. It occurred in Egyptians and in other foreigners but never, in my experience, in a Sudanese.

I saw every lunatic who was in confinement in all the large centres, making a clinical examination, including a laboratory study of the cerebrospinal fluid, and never encountered a single general paretic. On the other hand neurological manifestations of meningo-vascular syphilis were frequent, and routine examination of the cerebrospinal fluid at all stages of syphilis revealed a very high incidence of abnormal fluids, indicating invasion of the meninges.

My preliminary findings were published (*Brain*, 1932, **55**, 537), and prolonged subsequent investigations confirmed them. My conclusion was that the spirochaete reached the central nervous system as early as the primary stage of the disease in over 30% of cases and persisted there in over 20% at all subsequent stages: and yet there was no evidence of general paresis or tabes.

I take it that Dr. Marshall would distinguish between meningo-vascular syphilis on the one hand and true neurosyphilis (general paresis and tabes dorsalis) on the other. If that is so, I cannot agree that the incidence of the latter is not strikingly less in North Africans than it is in Europeans. There are some curious errors repeated in textbooks, but this is not one of them.—I am, etc.,

Bristol. T. F. HEWER.

## Eosinophils and Blood Clotting

SIR,—The paper by Dr. Z. Z. Godlowski (April 21, p. 854) and the letter from Drs. E. Keleman, M. Majoros, and T. Janovics (June 16, p. 1391) raise some interesting questions on the relationship of the pituitary-adrenocortical mechanism to blood clotting.

The work of Cannon and his school demonstrated that adrenaline, excitement, and pain decreased the clotting time, and a number of investigators have found shortening of coagulation time after the stress of operation (Bergquist; Rabinovitch). De Takats has reported that the eosinopenia after operation is accompanied by a fall in the heparin-delayed clotting time, which rises above normal if eosinopenia occurs subsequently. These observations seem to indicate that pituitary-adrenocortical activity results in an increase in coagulability of the blood, and this is borne out by the work of Cosgriff *et al.*, who found definite shortening of clotting time in 8 of 10 patients treated with A.C.T.H. or cortisone. They also note that of 175 patients so treated 11 developed thrombo-embolic incidents with two deaths from pulmonary embolism. The preliminary note by Smith *et al.* shows that, although A.C.T.H. and cortisone often produced an initial lengthening of coagulation time, this was usually followed by a decrease, and Godlowski also notes that A.C.T.H. was followed by a fall in clotting time in his control cases. Observations by the writer on five cases treated with A.C.T.H. or cortisone confirm that in general a decrease in the clotting time (Lee and White) and in the effect of heparin on the clotting time of recalcified plasma occurs in these circumstances.—I am, etc.,

Sheffield. J. V. GARRETT.

REFERENCES

Bergquist, G. (1945). *Acta chir. scand.*, **92**, Suppl. 101.
Cannon, W. B., and Gray, H. (1914). *Amer. J. Physiol.*, **34**, 232.
—— and Mendenhall, W. L. (1914). *Ibid.*, **34**, 243, 251.
Cosgriff, S. W., Diefenbach, A. F., and Vogt, W., jun. (1950). *Amer. J. Med.*, **9**, 752.
De Takats, G. (1950). *J. Lab. clin. Med.*, **36**, 817.
Rabinovitch, M. (1927). *Brit. J. exp. Path.*, **8**, 343.
Smith, R. W., Margulis, R. R., Brennan, M. J., and Monto, R. W. (1950). *Science*, **112**, 295.

## Preventive Psychiatry

SIR,—The morbidity figures quoted by Sir Allen Daley (June 9, p. 1279) forcibly underline what has been obvious to psychiatrists for some considerable time—namely, that "the psychoses and psychosomatic illnesses are probably the greatest single group of causes of unhappiness and inefficiency," and "that 48% of the hospital beds in the country are devoted to these illnesses." The actual incidence is probably much higher, as psychoneurosis often masquerades as colds, dyspepsia, headache, rheumatism, and so on. That 9.1% of those on the Disabled Persons Register suffer from nervous and mental disorders only stresses the urgent need for the employment of more psychiatrists and for preventive psychiatry. What is generally not known is that Dr. Minski at the Belmont Hospital has always emphasized the preventive aspects of psychiatry which form an integral part of the hospital's activities. Due to his untiring efforts and ungrudging help psychiatrists have been able to avail themselves of the guidance of a vocational psychologist and the services of officers of the Ministry of Labour, all of whom work in close co-operation and harmony to find suitable jobs for those patients who need them before they leave the hospital. The practical difficulties encountered in the rehabilitation of persons afflicted with some types of nervous illnesses have been pointed out elsewhere (*Proc. roy. Soc. Med.*, 1950, **43**, 517).

It is true to say that in psychiatry prevention and treatment are inseparable, as the one dovetails into the other; nevertheless a good deal of the minor degrees of psychoneurosis is wholly preventable. A unit at Belmont—the first of its kind in this country and associated with the work of Maxwell Jones—deals exclusively with the misfits in industry, and as "occupational therapy merges into therapeutic occupation" this unit fulfils an important function of prophylactic psychiatry. Other preventive measures discussed elsewhere (Pai, M. N., *British Medical Journal*, 1945, **1**, 289) are applicable to all patients convalescing from serious physical illnesses.

It would not, therefore, be difficult for those who have toiled in this field to suggest relatively inexpensive schemes for each region in which lay voluntary workers can also participate. In this connexion it must be emphasized that persistent insomnia and increasing irritability are the two very earliest manifestations of an impending nervous breakdown.—I am, etc.,

Sutton, Surrey. M. N. PAI.

## Paralytic Ileus after Hexamethonium

SIR,—Following recent letters in the *Journal* on paralytic ileus with fatal termination (June 9, p. 1331, and May 26, p. 1025) and hiccup treated with hexamethonium (May 19, p. 1143, and April 28, p. 948) we venture to report a case which we think is of interest.

A man aged 47 years was found to have hypertension 15 years ago during the course of examination for a life assurance policy. Two years ago he developed fibrillation and later congestive cardiac failure. He was treated with digitalis and "mersalyl," which improved him, but in February, 1951, his condition deteriorated with blood pressure of 260/160 mm. Hg and severe fibrillation necessitating complete rest. On March 20 we decided to treat him with hexamethonium bromide orally, and he was gradually worked up to 3 g. daily. His general condition improved, though it remained difficult to control the fibrillation, and he felt much better. His blood pressure dropped to 185/115. At the end of April supplies of the drug could not be procured and he had none for five days. On May 5 some tablets were procured and without our knowledge he began to take 3 g. again. On the next day he noticed that his vision was blurring and that he was dizzy, and later he developed colicky epigastric pains and diarrhoea. He then commenced to vomit, and was seen by one of us on May 7, blood pressure 145/90. When seen he appeared to be a typical ileus—pale, sunken facies, cold and clammy, weak thready pulse, marked abdominal distension with no borborygmi heard on auscultation, and copious bile vomiting. Hiccup was present. A Ryle's tube was inserted, and constant suction with fluid replacement was carried out for 24 hours. He was given "cedilanid" (gitoxin) intramuscularly and three-hourly "pituitrin" ½-ml. injections. The distension began to disappear by late night and occasional borborygmi could be heard. No urine was passed on this day. On May 8 the distension was much less, and by that evening had fully subsided. He passed 1 oz. (28.4 ml.) urine during the day and 10 oz. (284 ml.) during the night. The hiccup still remained in spite of all treatment and lasted for 11 days, though he had an occasional period of half an hour to an hour of relief. The blood urea on May 8 was 43.8 mg. The following day the bowels moved and the urine amount increased to one pint (568 ml.), and thereafter he steadily improved, though his blood pressure rose to 230/130 mm. Hg.

It is of interest to note that diarrhoea, not constipation, was a feature of this case, and incidentally of another patient at present under treatment, when the dose was increased above 2 g. daily; that ileus and such intractable hiccup could be traced directly to the hexamethonium; and that, if treatment should be stopped for any reason, it appears to be highly dangerous to resume with the full dose if given orally.—We are, etc.,

Ballinglass, Co. Wicklow. W. G. LYONS. P. J. LORD.

## Absorption of Hexamethonium

SIR,—Drs. J. G. Graham and A. Campbell in their letter (June 30, p. 1514) suggest, without any proof, that perhaps a greater percentage of an oral dose of hexamethonium dibromide is absorbed than has been found by Dr. S. Locket or ourselves (*Lancet*, 1951, **1**, 889). However, as a parenteral dose of hexamethonium is quantitatively (or almost so) excreted in the urine (an observation neglected by Graham and Campbell), surely it is reasonable to assume that there are no important destructive mechanisms in the body. Thus the urinary excretion after an oral dose is a measure of the amount absorbed. We agree that we cannot find all the remaining oral dose in the faeces, and we suggested that some destruction in the bowel may take place. In a recent experiment (unpublished) we have been able to recover, from both urine and faeces together, up to 70% of the oral dose. Of course, with high oral dosage, enough may be absorbed to give a hypotensive effect, but the variability in absorption makes this method of administration difficult to control.—We are, etc.,

G. E. MILNE.
S. OLEESKY.

Manchester Royal Infirmary.

## A Side-action of Methonium Compounds

SIR,—Drs. W. D. Wylie and H. C. Churchill-Davidson have broached some intriguing problems in their letter of July 7 (p. 54). It is scarcely surprising that the employment of induced vascular hypotension in surgical procedures should be accompanied by reduced general anaesthetic requirements, since a fall in blood pressure of sufficient degree in the conscious subject is followed by subjective changes of consciousness, and later coma, accompanied in certain circumstances by convulsions. The clinical picture is one of acute cerebral cellular anoxia, a condition which in itself is a potent, if primitive, form of anaesthesia.

As regards the observation of masseteric spasm following hexamethonium administration, it would be interesting to know the level of blood pressure at which this phenomenon occurred. Also whether "the generalized muscular weakness" experienced in four conscious volunteers was a subjective observation of diminished volition, or whether it had quantitative ergometric manifestations suggestive of neuromuscular block. Experiments carried out at Chichester on conscious subjects did not include ergometric studies, but subjective weakness appeared to follow the level of hypotension. For instance, in one normotensive subject weighing 86 kg. a dose of 240 mg. of pentamethonium iodide, given intravenously over a period of half an hour while reclining with a 35-degree head-up tilt, reduced the systolic pressure to 85 mm. Hg, and subjective feelings of weakness were present in slight degree only. On standing, however, the systolic pressure fell to 70 mm. Hg, accompanied by marked feelings of asthenia, anergy, and nausea, which subsided on resuming a reclining posture.

The investigation of hypotensive agents is a complex matter requiring careful controls to distinguish specific drug side-actions from the manifestations of cellular anoxia in cerebral tissue (and other organs associated with the maintenance of homoeostasis) which may accompany low blood pressures. To avoid confusing the particular with the general, parallel studies, using other methods to reduce vasomotor tone, will have to be undertaken in conscious subjects. This is a requirement which may naturally deter volunteers from accepting the full experimental conditions involved. For, while few in normal health would hesitate to undergo a short period of cerebral hypoxia induced by the relatively simple technique of intravenous hypotensive drugs (a procedure which in essence is no worse than a dental "gas," which many of us accept with gratitude), the longer time and relatively greater discomfort involved in techniques such as intra- or extra-thecal spinal block may prove deterrents to otherwise willing subjects.—I am, etc.,

P. R. BROMAGE.

Emsworth, Hants.

## Toxic Effect of Proguanil

SIR,—It is becoming increasingly evident to those of us who work in West Africa that, in susceptible persons, the choice of proguanil ("paludrine") as a malarial prophylactic has a number of disadvantages. The recommended effective daily dosage of 0.1 g. is taken by very large numbers of people without apparent ill effect. Short-term observations by various authors have been published (1945–9) on the toxicity of the drug, and the consensus of opinion has been that, even in the larger therapeutic doses, it has little or no toxic effect. But few investigations have been made of the chronic long-term toxicity of proguanil, though in the opinion of a number of observers loss of appetite and lack of energy have been manifest in those who have taken the drug for considerable periods.

It has been our experience that an impressive minority taking proguanil for long periods do suffer from toxic side-effects. There is, notably, a diminished sense of normal well-being, together with a loss of energy and appetite. There is often abdominal discomfort. There is also some reason to believe that the drug may have an effect on vestibular function. A number of cases have come to notice of episodes of sudden, inexplicable, and disconcerting loss of balance on change of posture. No complaint has been made of vertigo. On changing from proguanil to mepacrine patients have reported a disappearance of episodes of imbalance together with an enhanced vigour and a return of a normal sense of well-being.

In certain occupations, such as that of aircraft pilot, any interference with vestibular function, however slight, may well be attended with disaster.—I am, etc.,

P. C. COSGROVE.

Freetown, Sierra Leone.

## Prickly Heat and Heat Exhaustion

SIR,—It seems to me that the points of difference between Drs. G. O. Horne and R. H. Mole (July 14, p. 119) and myself will vanish if they accept my qualification of the case as one of mild heat exhaustion; possibly I erred in not emphasizing this mildness.

I concluded that the subject's heat tolerance was diminished, though certainly not "markedly," not because of changes in the sweat rate or sweat composition but because his rectal temperature rose more and he was more distressed on the second occasion he performed the standard test than on the first. Drs. Mole and Horne seem to suggest that the subject's heat tolerance may have been below par the first time he was tested (they could scarcely mean that it was increased when they query his condition); how much more remarkable, therefore, that his tolerance should be even worse some months later, after a hot season in Nigeria, coupled with duty in the climatic chamber, when his sunburn was healed and he was recovering from his prickly heat. The diminution in sweat production could not itself be the cause of the diminished heat loss; as I pointed out in my article, Thomson (1951) found that even grosser diminutions after ultra-violet irradiation did not affect heat tolerance; and it can be shown by using Powell's formulae (Bedford, 1948) that the maximum rate at which sweat can be evaporated from the human body under the conditions of this test is only 4 ml. per min. On both occasions the subject sweated at a greater rate than this and his unevaporated sweat was considerable.

The subject was not without symptoms; he complained greatly of his lassitude and debility even apart from his work in the climatic chamber, and it was only his loyalty and keenness that kept him going. He did not indulge in "strenuous exercise" in the heat at any time; during the tests his mean metabolic rate was 2 met (100 kg. cal./m.²/hour), equivalent to walking on the level at about 2 m.p.h.; and when on duty in the chamber his metabolic rate probably never averaged more than 1½ met. As for the "trying" conditions, although he was observing in climates up to 95° F. E.T. (35° C.) the average for the whole five months was only 90° F. E.T. (32.2° C.). In any case what is meant by "Normal or average severity"? I have recently carried out tests in an industrial concern where men were working regularly under even more severe conditions than those of

these tests. Surely it is all a matter of degree? Breakdown of adaptation will show itself first under severe stress only, later it will become apparent under less severe conditions. Selye himself in his work on animals which led to his concept of diseases of adaptation used stresses far from normal (Selye, 1948).

I congratulate Drs. Horne and Mole on their being able to obtain a series of figures on sweat from prickly-heat cases. Their observations that only the severe cases, when they develop mammillaria, show changes in the sweat chloride concentration tempt me to offer for discussion the suggestion that the train of events may possibly be as follows:

*Stage I.*—Individual has uncomplicated prickly heat. No effect on heat tolerance and no effect on sweat rate or composition.

*Stage II.*—Subject suffers from normal physiological fatigue, but prickly heat may get worse and mammillaria develop. The two together precipitate a mild degree of exhaustion, and signs of breakdown of adaptation to heat may be elicited by suitably designed severe tests (as in the present case). The man, though tired, can carry on.

*Stage III.*—With continuation of prickly heat or prolongation of heat stress the exhaustion increases. Sweat rate is sensibly diminished and lowered heat tolerance is indicated by an undue rise in the body temperature during the day. The man can carry on until mid-day.

*Stage IV.*—Complete breakdown of adaptation with fully developed Type II heat exhaustion and indications of mineralocorticoid deficiency. The man becomes a casualty.

On this hypothesis bad prickly heat is the "last straw" that precipitates the breakdown, and the changes in sweat rate and composition and in heat tolerance are secondary to the breakdown, not to the prickly heat itself. Perhaps Drs. Horne and Mole would like to say whether this would fit in with their Karachi observations? If this hypothesis is accepted, then the question of the differentiation clinically between prickly heat and heat exhaustion Type II becomes meaningless; they are two distinct conditions, but the former may predispose to the latter. It is also conceivable that Type II exhaustion could be precipitated by other factors than prickly heat; indeed, in Iraq we did see some cases where the history of prickly heat was not quite clear (unclassified cases).—I am, etc.,

Oshodi, Nigeria. W. S. S. LADELL.

REFERENCES

Bedford, T. (1948). *Basic Principles of Ventilation and Heating*, p. 19 London: Lewis.
Selye, H. (1948). *Ann. Intern. Med.*, **29**, 403.
Thomson, M. L. (1951). *J. Physiol.*, **112**, 22.

## Anatomical Atlases

SIR,—Would Professor Harris please explain a part of his entertaining review of "Anatomical Atlases" (June 16, p. 1368)? He "tests" an atlas of anatomy by its depiction of the mandibular branch of the facial nerve, demanding that it "descends into the neck and then climbs up on the mandible." In competition with the written word, any anatomical illustration is at a disadvantage, since it can neither be ambiguous nor suggest alternatives, but surely an atlas of normal anatomy, unless unlimited in scope, can do little more than present the normal despite the significance of a variant. I am not clear, however, whether Professor Harris is suggesting that his description is in fact the normal. If this is so I would be glad to know of any published figures supporting this argument, as all references I have checked suggest that in some 60% of cases the mandibular twigs run wholly above the lower border of the mandible, and that in the majority of the remainder if a filament descends below the angle of the jaw it is only one of a reduplicated series, the others of which are situated higher. Even in the books which Professor Harris commends (Gray's *Anatomy*, 1858, and Quain's *Anatomy*, 10th ed.) the illustrations as well as the text "fail" by the "test" he applies.—I am, etc.,

Aberdeen. GILBERT F. HAMILTON.

SIR,—In reply to the letter of Mr. G. F. Hamilton which is printed above, I refer him to the atlas by Joseph Swan (1834) in which the "inframandibular" position of the mandibular division of the facial nerve to the muscles of the lower lip is correctly displayed. More recently Hovelacque (1927), quoting Lagrot, gives the distribution as:

Eleven times the nerve ran along the lower border of the mandible.

Eight times the nerve ran from 1 to 3 mm. above the lower border of the mandible.

Fifteen times the nerve ran below the mandible in the submandibular triangle, the summit of the curve being distant from the mandible by a distance ranging from 2 to 12 mm. Moreover, on many occasions the nerve was in close contact with the lymphatic glands of the area.

Lagrot (1924) himself suggests that any incision in the area should be 2 cm. away from and parallel to the lower border of the mandible with the head in extension.

I do not "demand" that the mandibular branch of the facial nerve should descend into the neck and then climb up on to the mandible. I used this nerve "as a test of the need for precise anatomy in relation to clinical significance." Mr. Hamilton should give his statistics some air of verisimilitude by stating the number of cases examined. You can cook a 60% result on five dissections.

Repeatedly one sees children with a paralysis of the muscles of the lower lip as a result of section of this nerve following the opening of an abscess. They are not a pleasant sight for their friends when speaking, chewing, or drinking.

The diagram referred to by Hamilton in Quain's *Anatomy* is third hand, "from Sappey, after Hirschfeld and Leveillé." The incorrect diagram in Gray's *Anatomy* by H. V. Carter has remained unchanged since 1863—the earliest edition to hand.

Careless anatomical teaching may be held responsible for many surgical disasters. The branches of the facial nerve have a tendency to lie superficially, to run obliquely to the accepted lines of incision, and to hide their identity, for they are thin and flat rather than round, ribbon-like rather than cord-like. They escape the eye but not the scalpel.—I am, etc.,

Anatomy School, Cambridge. H. A. HARRIS.

REFERENCES

Hovelacque, A. (1927). *Anatomie des Nerfs Craniens et Rachidiens et du Système Grand Sympathique chez l'Homme*, p. 186 *et seq.* Doin, Paris.
Lagrot, F. (1924). "Recherches sur la Topographie de la Branche Cervico-faciale," *Bull. Soc. Anat. Paris*, **94**, pp. 159-68.
Swan, Joseph (1834). *A Demonstration of the Nerves of the Human Body.* Longmans, London. Plate xiv, Fig. 1.

## American Impression

SIR,—Two years ago (June, 1949), following a visit to America and Canada, I wrote in your journal:

"In my 1947 letter I spoke of the exceptionally adequate laboratory and research accommodation both for animal experiment and human metabolic studies that I had met with. This year I saw the foundation of a 500-bed hospital where the additional planned space for investigation and research is twice that for bed accommodation. Many of us hope, in spite of initial financial stringency, that the National Health Service will give us such facilities in our major hospitals and that plans for the future will be courageous and with vision. Space alone, however, does not necessarily determine good research, and there is no lack of appreciation in America of the fundamental character and high quality of research in this country, and of the clinical-pathological background on which our methods of medical education produce sound results."

Having just returned from fulfilling invitation lectures at the New York Academy of Medicine and at Los Angeles, I feel that this paragraph bears repeating and emphasizing. On the West Coast the development of the medical school of the University of California is proceeding along lines which, recognizing the modern trends in medical advancement, are giving adequate facilities, space, and personnel for the ancillary sciences to enter and be linked with the medical ward. The same is true of the Veterans Government Hospital at Long Beach, where the application of physics and physical chemistry is very highly developed. In the University of Minneapolis, the new Heart Hospital, built under the wise guidance and forward look of Professor McQuarrie, has extensive facilities for laboratory investiga-

tions of a character well outside more immediate cardiac problems. Similar developments are occurring in Canada, where the new Children's Hospital in Toronto excels one's dreams.

In this country, most hospitals with plans for expansion or rebuilding have had to exercise restraint because of the stringency of Treasury control and the limitations on building projects. All this may well be completely justified by overriding national considerations and is thus accepted; and it is recognized that hospital finances under the voluntary system might well have proved inadequate. Nevertheless, the intrinsic urgency of hospital clinical and research requirements must not be lost sight of, and the pragmatic needs of the moment must not cause modifications of plans in such a way as to ignore the changing character of medicine and the impact of the ancillary sciences on its practice as well as on fundamental research. As expansion and reconstruction become feasible we must remember to build for the future as well as for the present.

Another type of contrast is noticeable in the availability of the relatively new and expensive hormones cortisone and A.C.T.H. In the U.S.A. and Canada there appear to be sufficient supplies to permit an enormous number of research workers to attack along a broad front, using these substances as new weapons searching out for points of advancement. In this country, supplies, now slowly improving, have been more like a trickle, perhaps not inappropriately filtered through the Medical Research Council to chosen centres and to individuals who can state precisely a line of research that appeals to the M.R.C. expert Advisory Committee.

However, the concluding sentence of my paragraph holds good; and in endocrinology the work of F. G. Young at Cambridge on growth hormone and diabetes, and that of Bornstein and Lawrence at King's College Hospital on the measurement of plasma insulin in man, using the alloxan-treated hypophysectomized-adrenalectomized rat, has been highly appreciated in America. To these achievements we might well add the recent fundamental work of D. A. Long and colleagues at the National Institute for Medical Research on the mechanism of action of cortisone and the part played by the oxidation products of ascorbic acid.—I am, etc.,

London, W.1. S. LEONARD SIMPSON.

## Prevention of a Coronary Thrombosis

SIR,—Dr. Rae Gilchrist in the *British Medical Journal* of April 21 (p. 874) and April 28 (p. 937) has given us a thorough and learned article on "Coronary Arterial Disease" with its treatment; but he has not told us how to prevent a coronary thrombosis, which is perhaps the greatest medical scourge of this century, for it has increased by 900% in the last 30 years in civilized countries.

Dr. Gilchrist has stated that we know no method or treatment to prevent it—e.g., by drugs or diet, etc.—but we have two factors to help us in prevention; the first is that the complaint is nothing like so prevalent among labourers, and the second is that surgeons order deep breathing after any serious operation to prevent thrombosis of the leg, which brings with it the risk of an embolus being detached and carried to the heart, lungs, or brain with the possibility of a fatal issue, the deeper breathing producing a larger flow of blood through the vessels of the leg with more oxygen and thus reducing the risk of a thrombosis followed by an embolus. Before the operation the surgeon now sends an instructor to teach the patient how to breathe correctly and thus more deeply. In the case of a labourer there is a more rapid flow of blood through all the vessels of the body, and the blood in addition has more oxygen, and this combination, it is suggested, would keep the lumen of any blood vessel healthier and thus lessen the risk of arteriosclerosis, etc., and a coronary thrombosis. It is safe to say that we doctors when we examine a patient do not know whether he is breathing correctly, and if we think he is not we do not know how to teach him to do so. What we want to aim at is to get the floating ribs to move and thus ensure that the diaphragm is working correctly and thus producing more rapid flow of well-oxygenated blood.

The following is a certain method of ensuring perfect breathing with the floating ribs moving; push head straight up gently, the head facing horizontally to the front; slight flexion (high up) of head on neck (gently); learn to do this simultaneously; drop shoulders; feel the heels as well as the ball of the toes when standing and sitting. These exercises are important but really simple to do.—I am, etc.,

Ealing, W.5. R. HALSTEAD DIXON.

## Polymastia and Lactation

SIR,—With regard to the letters (May 12, p. 1060; June 2, p. 1264) on this subject, in about 1934 I anaesthetized an adolescent girl for my partner to remove a developing accessory breast on the buttock. Its tenderness when touched or knocked during games at school required its removal. It had a well-formed nipple and penetrated about 1½ in. (3.7 cm.) into the gluteal muscles, and was about this length in diameter. The wound healed normally.

When I was senior medical officer at Crumpsall Hospital in 1931 a case was confined under my charge which had three accessory breasts in the midline of the axilla, and also an accessory breast below the normal nipple line. They all lactated normally in a small way.—I am, etc.,

Bridgwater. R. FREER SHEPPARD.

## Medical Practice on the Gold Coast

SIR,—By the passage of the Medical Practitioners and Dentists Registration (Amendment) Ordinance No. 30 of 1950 through the Legislature of the Gold Coast Colony last year, a far-reaching and retrograde step was accomplished. The objects and reason of the Bill as stated are to permit the licensing as medical practitioners of persons "not entitled to practise medicine, surgery, and midwifery in the United Kingdom provided they hold, or have held, a diploma granted in *any place* outside the United Kingdom."

Until the passage of this Ordinance, all registered medical practitioners—African and European, Government and non-Government—had to possess one of the registrable qualifications recognized by the G.M.C., and to this rigid requirement can be attributed the high standard of work and ethics that the Colony has enjoyed hitherto.

Notwithstanding the strong opposition put up in the Legislature by the doyen of the African medical practitioners, this Bill was passed on the grounds that wherever the Director of Medical Services was satisfied that any place had insufficient medical practitioners to meet the needs of persons in such place he might grant licenses under the new Ordinance. Since there are only about 100 registered practitioners to serve six and a half million people, no area in the Gold Coast can be said to be sufficiently doctored, and thus a wide-open opportunity has been legally granted for the introduction of foreign practitioners. This process has already begun, and has had three immediate effects.

First, it has reduced the pride of the African practitioner in his hard-earned English qualification, since he now finds that he might just as well have taken some foreign modified or Colonial qualification in shorter time and at less expense. Secondly, it has introduced a new class of doctor at enhanced rates of contract pay and with entirely different standards of treatment and ethics from those previously current in the Gold Coast. This gravely penalizes doctors, both African and European, who joined through the Colonial Medical Service in the normal manner. Thirdly, by "dilution" it has obstructed the members of the Service in their struggle for better standards of pay and conditions.

That the lay members of the Senior Civil Servants' Association, both African and European, regard this as a retrograde step is shown in their published "Recommendations" to the Lidbury Commission in November, 1950. I quote:

> By "dilution" is meant precisely what the British miner means by the term—namely, the introduction into a trade or profession

of relatively unskilled recruits or trainees who are prepared to accept lower wages than fully qualified workers, and whose presence thus reduces the salary value of their fully qualified colleagues.

A classic example of "dilution" is the recent amendment to the Medical Ordinance whereby doctors not admissible to the British *Medical Register* may obtain licences to practise in the Gold Coast. Central European refugees may thus be employed here although the General Medical Council considers them unfit to practise in England. If this Government is successful in attracting such people there will be no necessity to offer salaries and conditions which will tempt British and African doctors to enter the Service: that conditions and salaries are not at present sufficient inducement may be inferred from the extreme shortage of staff in the Medical Department, and from the number of African doctors of Gold Coast origin who prefer to practise in England rather than in their native land. It is unlikely that young British doctors will join or remain in a Service where their colleagues, whether from Europe or the U.S.A., are not considered adequately qualified, and the amended Ordinance is unlikely in the long run to fulfil its purpose of increasing the appallingly inadequate number of doctors in the Colony. If the Government will pay British or African doctors the proper rate for the job, they will come here, otherwise the shortage will remain unrelieved.

To those whose professional life has been devoted to building up a coherent Service in the Gold Coast this new Ordinance is heartbreaking. To those now in their prime, and to whom a future in the Service seemed desirable, the Ordinance is a devastating blow. Nor is this all. By a Statutory Powers and Duties (Transfer to Ministers) Order No. 64 of 1951, the Minister of Health and Social Welfare of the Gold Coast is now able to remove persons from the Register of Medical Practitioners, whereas previously this power was held only by the Governor in Council. The true cost to the Colony will be realized only when all regularly qualified practitioners have left the Service—as they undoubtedly will do at the earliest opportunity—in the face of what can be regarded only as a disastrous lowering of medical standards.

As, under the Pensions Ordinance of the Gold Coast Colony, pensions are not of right but only at the behest of the Legislature, I greatly regret that I am compelled to seek sanctuary in the anonymity of your columns, enclose my card, and sign myself

GOLDCOASTER.

## POINTS FROM LETTERS

### Thought and Terminology in Anaemias

Dr. J. P. MCGOWAN (Aberdeen) writes: I read with great interest Sir Henry Dale's lecture (July 7, p. 1). . . . He states that "recently came the isolation of the active principle deficient in that disease," with the implication apparently that this deficiency was the cause of the disease. The opinion of Sir Henry on any medical scientific question is, of course, worthy of respect, and it is because of this that one wonders why he lends his support to a view so much at variance with the well-founded theory originally propounded by Ehrlich. Moreover, Dr. Lester Smith (p. 50) makes reference to substances other than vitamin $B_{12}$ which are active in this sphere: and because I hold this multiple view, when I have occasion to refer to them, I use the non-committal collective term "liver-agent." . . .

### Fainting on Parade

Mr. B. R. SWORN (Stone, Staffordshire) writes: I have read with interest the recent correspondence in *The Times*. . . . Dr. Sharpey-Schafer puts what seems to be the modern medical view on fainting . . . but does it really account for the facts? Does severe haemorrhage always cause the bed patient to "faint"? Is fainting always preceded by a fall in the general blood pressure? Has the body no defence against "standing to attention" so that the old soldier really is an unphysiological phenomenon? Has fear [of punishment] no effect on the circulation? Is it no longer true that anaemia of the brain may be due to local reflex arterial contraction, among the causes of which emotion and posture are not the least important. . . .

# Obituary

## SIR WALTER JOHNSON, C.M.G., M.B., F.R.C.S.

Sir Walter Burford Johnson, whose death, at the age of 65, was recently reported from Capetown, was one of the outstanding members of the Colonial Medical Service.

From the City of London School he went on to St. Thomas's Hospital, where he took the conjoint qualification in 1908 and in the succeeding year the London M.B. In due course he was appointed surgical registrar at his hospital, and in 1911 he became F.R.C.S. He seemed destined to follow a surgical career, but in 1912, to the surprise of some of his friends, he joined the West African medical staff. Shortly after his arrival in West Africa he was seconded for service under the Yellow Fever Commission, and some of his work is recorded in the reports of that Commission, which unfortunately came to an untimely end with the outbreak of the first world war. He saw active service in the short-lived campaign in the Cameroons in 1914 and 1915, and then returned to Nigeria, where the gravity of the threat of sleeping sickness was just being recognized. In 1921 he was appointed to the tsetse-fly investigations in Northern Nigeria, and the next few years with their admixture of field work and laboratory studies were probably the happiest in his life. With Lloyd and Ramson he published a number of papers on the behaviour of trypanosomes in tsetses, and in addition he successfully organized measures for the diagnosis and treatment of sleeping sickness. In 1929 he became Director of Medical and Sanitary Services in Nigeria, and for seven years he controlled the public health of the largest colony in the Empire. He received the C.M.G. in 1933, and a year before his retirement in 1935 he was knighted. His work on trypanosomiasis had convinced him of the importance of thorough scientific study of all aspects of the tsetse problem if this menace to the lives of man and his domestic animals were ever to be conquered. With this aim in view additional scientific staff were engaged and investigations were begun on a wide front. Before the work could come to fruition the financial crisis of the early 'thirties seriously curtailed the scope of the studies. Nevertheless, the scientific study of sleeping sickness had been begun, and the present Trypanosomiasis Research Institute at Kaduna is the direct descendant of this early scheme. After his retirement Johnson did not desert Africa, but after a short period in Europe he went out to Basutoland as superintendent of the Botsabelo Leper Institute at Maseru. At the time of his death he was working in Pretoria as medical adviser to the High Commissioner for Basutoland, Bechuanaland, and Swaziland, where he was doing much to improve health conditions.

Johnson was essentially a field worker, and he was at his best when on trek. He was prepared to drive his truck over any road or no road, and, accompanied by his sister, he thought little of starting from Lagos and driving across Africa to England. He was a keen fisherman and a strong swimmer, though when no longer in his first youth he nearly lost his life in gallantly attempting to rescue a friend from the treacherous breakers of the Lagos beach. At the Centenary Meeting of the British Medical Association in 1932, Johnson presided at some of the meetings of the Section of Tropical Medicine.

## WILLIAM IRVING, M.D., M.R.C.O.G.

Dr. William Irving, who was honorary physician to the Christchurch Hospital, New Zealand, for many years, died on May 28 at Totland Bay, I.W., aged 81.

William Irving was born in England, but went with his father, Dr. James Irving, as a boy, to Christchurch, New Zealand. He was educated at Christ's College, New Zealand; Caius College, Cambridge; and the Middlesex Hospital. Qualifying in 1895, he graduated M.B., B.Chir. in 1897 and proceeded M.D. in 1911. After holding the posts of house-surgeon and house-physician at the Middlesex Hospital he returned to Christchurch, where he was appointed honorary physician to the hospital and remained in practice until 1934. A foundation member of the Royal College of Obstetricians and Gynaecologists, he was for many years external examiner in midwifery to Otago University and at one time was president of the New Zealand Obstetrical Society. He was also first chairman of the New Zealand Medical Council. A leading member of the B.M.A. in New Zealand, he was president of the Canterbury Division of the New Zealand Branch. In 1921, 1934, and 1942 he attended the Annual Meetings of the B.M.A. in this country as a representative of the New Zealand and Fiji Branches. During the first world war he served with the R.A.M.C. and the N.Z.M.C. When he returned to England in 1934 he settled in Winchester. He continued his work for the B.M.A., and was a member of the Central Council from 1938 to 1946 and of the Dominions Committee from 1933 to 1946.

Dr. Douglas Anderson writes from Christchurch, New Zealand: To those who were privileged to know Dr. William Irving the news from Britain of his death caused much sadness. "Silent Bill," as he was familiarly known to his colleagues and to many of his patients, was a most likeable man. His knowledge and love of his profession were great, and he was deservedly the idol of his family and his patients. Dr. Irving's quiet sense of humour was very evident when, on handing over his practice to me before returning to England, he said: "For 30 years I have been getting out of bed for other men's wives; I think it's time I went home!" His practice in obstetrics was of a very high standard. Old-world courtesy together with a commanding appearance and unexcelled bedside manner are attributes inseparable from one's memory of William Irving. A staunch Churchman, he was what one might safely call the perfect family doctor, that rapidly disappearing "backbone" of the profession of medicine.

## HENRY M. JOHNSTON, F.R.C.S.

Mr. H. M. Johnston, honorary consulting surgeon to the Royal Victoria Infirmary, Newcastle-upon-Tyne, died at his home after a brief illness on June 22, at the age of 74.

Henry Mulrea Johnston, the son of a general practitioner, was born at Holywood, County Down. He studied medicine at Queen's College, Belfast. After a brilliant career, in which he carried off scholarships year by year, he graduated M.B., Ch.B. (R.U.I.) in 1903. These successes led him to think of an academic life, and in 1904 he went to Trinity College, Dublin, as demonstrator in physiology under Professor William Henry Thompson. The study and teaching of anatomy attracted him, and later that year he became chief demonstrator in anatomy at Trinity—a post which he held until 1910. These were fruitful years, for he combined research with teaching. The anatomical museum at Trinity College still preserves the beautiful plaster models of the carpal bones which he made to illustrate one of the several papers he wrote at about this time. His chief, Professor A. Francis Dixon, recognized the fertility of his genius and had high hopes of a professorial chair for him, but the practical application of his studies turned Johnston's attention towards a clinical career. He therefore left Dublin in 1910 for London, where he studied medicine and surgery during the next two years, mainly at the London and St. Bartholomew's hospitals. He became a Fellow of the Royal College of Surgeons of England in 1911 and worked as a clinical assistant first at St. Bartholomew's and later at the Hospital for Sick Children, Great Ormond Street. With this background he gained the appointment of resident medical officer at the Royal National Orthopaedic Hospital early in 1912, and later in the same year he obtained the post of resident medical officer at the Royal Victoria Infirmary, Newcastle-upon-Tyne.

When the war came in 1914 he soon found himself surrounded in the "House" by student-residents, with the added responsibilities of supervising their work, of helping them with emergencies of all kinds, and of teaching them practical medicine and surgery. With a depleted senior staff many tasks fell to his lot, and he was one of the first, if not the first, to administer gas, oxygen, and ether as a general anaesthetic in the hospital. Realizing the potentialities of radiological diagnosis he set out to learn all he could about electrical transformers and *x*-ray tubes, and he built up an *x*-ray plant of his own which he used with modifications throughout the rest of his professional life. In 1917 he joined the R.A.M.C. and was posted to the Queen's Hospital, Sidcup, then devoted to the treatment of injuries and deformities of the face. This was work after his own heart, and there, in association with the surgeons who were tackling the new problems of plastic surgery, he laid the foundations of techniques which enabled him to make his original and fundamental contributions to knowledge of the jaws a few years later.

Soon after his return to Newcastle he had the great satisfaction, in 1920, of being elected honorary assistant surgeon to the Royal Victoria Infirmary, and about this time he was also appointed visiting surgeon to the Children's Sanatorium at Stannington, near Morpeth. The surgery and radiology of bones now claimed his major interest. In general surgery he loved to demonstrate bone tumours and cysts and to illustrate his cases with beautiful radiographs of his own taking. To avoid the introduction of metal, when he found it necessary to operate on a fractured bone he substituted absorbable plates, bolts, and screws of bone made in his own workshop—with most satisfactory results. He used a suspending gallows for the application of plaster jackets for the first time in the Infirmary. As a clinical teacher he was lucid and stimulating. His cases were carefully chosen and covered a wider range of surgery than the specialties now permit to the general surgeon. He delighted in the dramatic, and no one enjoyed his own eccentricities more than himself. Dental surgeons also sought his help, and he began to devote considerable attention to the surgery of the face, writing three important papers on the subject. He became honorary surgeon to the Infirmary in 1927, and for the next 10 years he continued to serve the hospital in his own inimitable way. In later years his help was constantly sought in compensation and medico-legal work, and in this he found great scope for the exercise of his talents.

In 1928 he married Muriel, the eldest daughter of his first chief at Trinity (the late Sir Henry Thompson), and established a country home where he was able to indulge his great love of gardening.

J. G. writes: Johnston had the Irishman's tact, geniality, and attractiveness in good measure. Those of us who were resident at the Royal Victoria Infirmary when he was R.M.O. were fortunate to have such an able and attractive personality as our own particular guide, philosopher, and friend. The hospital and the people of the North of England owed him a great debt of gratitude for his selfless devotion and sterling worth. He was regarded with universal respect, and his love of fun and ready wit endeared him to us all and earned for him the affectionate name of "Pa J." It was typical of his humility that he chose to present his important work on the surgery of the face to the dental rather than to the surgical profession, for he never sought the limelight of the successful, but was content to hand on the fruits of his labours to those who would profit most from them. His upright character, his sense of honour, and his sense of humour stamped him as one of Nature's gentlemen. Never seeking social prominence or great financial rewards, he was content to serve his day and generation with all his skill. His shrewdness and his wide knowledge gave him judgment of a high order, while his kindliness made him a friend to all. His was the modesty of the truth-seeker and the wisdom of those who endure to the end. He leaves a widow and two sons, and to them we would extend our sincere sympathy in their bereavement.

### IVOR BACK, F.R.C.S.

Dr. G. F. Newbold writes: It is with deep regret that I read of the death of Mr. Ivor Back (*Journal*, June 23, p. 1452). It was my great privilege to be his house-surgeon at St. George's—and what an enjoyable experience this was. He once told me, towards the close of his long and distinguished career at "the Corner," that one of his proudest recollections was that never once had he had a row with his house-surgeon, and I can well believe this to be so. His tall, commanding presence and striking personality, which so often had an elevating effect on the spirits of his patients—and his colleagues—were indeed worthy of his ancestor, the first Duke of Wellington, to whom he bore a physical resemblance. Whenever one met him there was the ever-ready spontaneous friendly smile and greeting which would banish gloom and depression, although if convinced of the justice of any cause he could, should it become necessary, prove a most formidable and courageous opponent. Truly a "good companion," his loss has caused a gap which it will be difficult to fill, not only at St. George's but in a much wider sphere outside.

---

Dr. LACHLAN GRAHAM CAMPBELL, who had practised in Earlston, Berwickshire, for over 25 years, died in Edinburgh on June 24 at the age of 58 after a brief illness. He was born at Balloch, on Loch Lomond, and spent his early life in North Berwick. Intent on studying divinity, he entered Edinburgh University, graduating M.A. in 1914. At the outbreak of war he joined the Royal Artillery, rising to the rank of major. He was awarded the *M.C.* and was mentioned in dispatches. His war service turned his mind to medicine, and he took this up on his return. He graduated M.B., Ch.B. at Edinburgh in 1924, and after holding a house-surgeon's appointment at the Royal Infirmary he went to the Borders as assistant to Dr. Young, later taking over the practice when Dr. Young died. Lachlan Campbell loved his work and his patients, and his devotion and kindliness will long be remembered by them. His work on behalf of his colleagues and the B.M.A. was likewise a great example. He was Chairman of the South-Eastern Counties Division from 1934 to 1935 and again from 1946 to 1947, serving also on the executive committee. As a member of the local medical war committee, the rural practitioners' committee, the local executive council, the local medical committee, and the Guild committee, as well as the Dingleton Hospital management board, he gave much constructive thought to medical administration. His last illness began as he was about to go to London as the representative of the Division. A fine golfer, he more than once played for the Treasurer's Cup, and in recent years became an enthusiastic photographer. His unexpected death was a great blow, and the very large attendance at the service at Warriston Crematorium was a fitting tribute to the esteem which he so richly merited. He is survived by his widow and three boys, to whom our sincerest sympathy is extended.—A. S.

## Medical Notes in Parliament

### Payments to Chemists

On July 11 Mr. HUGH LINSTEAD drew attention to the publication of revised Civil Estimates where the amount for the pharmaceutical service had increased from £34,500,000 to £43,500,000 since February. He calculated that just before the Service came into force 90,000,000 prescriptions a year were dispensed in chemists' shops in England and Wales. By 1950, 225,000,000 public and private prescriptions were dispensed in roughly the same number of chemists' shops. The chemists had shouldered that burden with no breakdown by enlarging in advance their dispensaries and increasing their staffs. The breakdown had occurred in the Government pricing offices, which had frankly collapsed under the task. Mr. Bevan had estimated that in 1949 the pricing offices would have to deal with 140 million prescriptions. In fact they had that year to deal with 187 millions. During the past 12 months the price of drugs had gone up steeply. At present the Minister owed the chemists about £4m.—an average of about £300 to each chemist's shop—and was getting about six weeks' credit from the chemists of the country. Unless the Ministry could come back to something like detail pricing it would never be in a position to check the small number of doctors who were over-prescribing. A return to accurate and early pricing was essential to the service. He was sure that the expenditure of £35,500,000 on prescriptions must be a stimulus to the Ministry to wean the public from a desire to take medicine and to get them to understand the principles of maintaining health by other means.

Dr. CHARLES HILL said that some of the difficulty was due to the enormous increase in the work falling on the pharmaceutical service. In 1949 the cost of pharmaceutical services in Great Britain had been £17,750,000. The present estimate was for £43,000,610. The general-practitioner service as a whole cost about £48m. If the charge for the pharmaceutical service continued to rise, the additional money would have to be found by corresponding reductions in other parts of the service. Five prescriptions were given every year for every man, woman, and child in the country. The cost of prescriptions doubled between 1947 and 1950 as a result of increased cost of ingredients. The Minister, with the aid of the Cohen Committee, had gone a long way to tackle the problem of practitioners' prescribing. He had maintained the freedom of the practitioner to prescribe what he believed to be necessary, and at the same time had given advice through the Cohen Committee which would have the effect of bringing down the cost of this service. The real solution of the problem could lie only in a different attitude towards health. Dr. Hill said he believed that the only effective way of discerning such excessive prescribing as existed was to return to the pricing of prescriptions and the calculation of individual average cost, but that procedure was impossible until the individual costing of prescriptions was restored.

Dr. H. B. W. MORGAN said that some doctors who criticized over-prescribing had never been in the midst of medical practice as it concerned both doctors and patients. Members had spoken discouragingly of proprietary medicines, but many of these medicines were the result of recent research, and some doctors thought it right to prescribe them although they were expensive. It must be left to the doctor to prescribe a suitable drug under the Health Service, whether it was costly or not.

Mr. HILARY MARQUAND said the revised estimates had been necessary because the first ones had been put forward when the Government had not decided precisely where the charges were to fall. The revised estimates made no difference to the overall saving which the Government would get. Until recently pricing bureaux were not able to price prescriptions as fast as they received them, but they were now pricing them at the rate of receipt. Arrears were no longer accumulating, and substantial payments had been made to the chemists. The Ministry was not far from paying the chemists regularly as much money as they would have received if the pricing system had been perfect. The Ministry should sit down with the chemists and find a way to eliminate the whole of the arrears.

A division was challenged, and the estimate was carried by 257 to 233.

### School Medical Officers in Durham

On July 12 Mr. M. C. HOLLIS asked how many vacancies there were at present for assistant school medical officers in County Durham, on what conditions those posts had been offered, and how many applicants there had been for them. Mr. G. TOMLINSON, in reply, said the local education authority had at present vacancies for four assistant school medical officers. So far as his information went the conditions attaching to these posts were those stated in the advertisements—namely, three years' experience in practice and the possession of the diploma of public health. One application had been received. Mr. Hollis further asked whether the advertisement indicated that the salary offered was £150 less than that in the Industrial Court's award of December. Mr. Tomlinson said he thought that to be true.

Dr. CHARLES HILL inquired whether Mr. Tomlinson was aware that the closed-shop resolution still applied to the post of assistant school medical officer, in addition to the failure of Durham County Council to implement the award of the Industrial Court. Mr. TOMLINSON replied that this was not in the advertisement.

### Social Survey of Sickness

Mr. F. J. ERROLL, on July 12, asked what specific results accrued from the Survey of Sickness being carried out by the Social Survey, how much it had cost, and for how long it was expected to continue.

Mr. H. MARQUAND answered that by means of the Survey of Sickness new and valuable knowledge had been and was being obtained about the volume and nature of the illness and injuries of all degrees of severity among the adult population in England and Wales, about the amount of time lost from normal activities on account of sickness, and about the amount of medical attention involved. The estimated cost of the survey in the current year was £28,000. He added that owing to changes in organization and procedure it was not possible to state separately the total cost in the seven years of its existence. It continued to provide necessary information not otherwise obtainable.

---

*Consultants.*—At the end of 1950 about 1,500 consultants in England and Wales were employed whole-time and about 4,100 part-time. Mr. Marquand was unable to state the gross remuneration earned by either class.

*Cortisone.*—Mr. Marquand reported that 56 hospitals in England and Wales receive monthly supplies of A.C.T.H. and cortisone.

*Ambulances.*—Seventeen local authorities have adopted the system of radio-controlled ambulances. Eight others are introducing it.

*Vitamins.*—The number of vitamin tablets dispensed daily through the National Health Service is estimated at about 500,000.

# Medico-Legal

## LABEL NOT A FALSE DESCRIPTION

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

New Era (Laboratories) Ltd. were recently summoned[1] before the Liverpool magistrates at the instance of the Crosby Borough Council in respect of descriptions of "nervone" in an advertisement and on labels. Boots Cash Chemists Ltd. were also summoned for selling "nervone" under similar labels, but it was stated on behalf of New Era (Laboratories) Ltd. that if an offence had been committed they, as manufacturers, would accept full responsibility.

The matters complained of as "false descriptions" in the advertisement and labels were that a bottle of "nervone brain and nerve regenerator tablets" bore the words "for vim, vigour, and vitality. . . . It contains one of the most potent nerve nutrients known to modern science." Dr. W. H. Race, of the Home Office, said in evidence that "nervone" contained 99.7% lactose and 0.3% inorganic matter. The words "brain and nerve regenerator" meant practically nothing to him, and he saw no reason to call lactose a nerve regenerator, while there was too little of any other component to matter.

Mr. Glyn Jones, K.C., for the defence, observed that the medical profession would like to drive proprietary medicines out of existence, but people were free to buy them if they wished and to use their common sense in considering claims made for them. He called Dr. Henry Edward Cox, who said in evidence that he had analysed "nervone" and found the label on the bottle to be completely accurate. Dr. Francis James Wheeler, who had practised homoeopathic medicine for 49 years, gave evidence that all the ingredients mentioned on the "nervone" labels were recognized homoeopathic medicines.

The magistrates dismissed all the summonses.

---

[1] *Manchester Guardian*, February 24.

# The Services

Major D. H. R. Montgomery, M.C., has been mentioned in dispatches in recognition of gallant and distinguished services in Korea.

The President of the U.S.A. has conferred the decoration of Legion of Merit, Degree of Officer, upon Lieutenant-Colonel G. T. Hankey, O.B.E., T.D., R.A.M.C., in recognition of distinguished service in the cause of the Allies during the 1939–45 War.

The King of Denmark has conferred the decoration of Commander of the Order of Danebrog, 2nd Class, upon Lieutenant-Colonel R. W. Scott, O.B.E., R.A.M.C., in recognition of distinguished service in the cause of the Allies during the 1939–45 War.

A *Supplement* to the *London Gazette* has announced the following awards:

*Four Clasps to the Territorial Efficiency Decoration.*—Majors (Honorary Lieutenant-Colonels) R. S. Creed, T.D., and C. W. Healey, M.C., T.D., R.A.M.C.

*Three Clasps to the Territorial Efficiency Decoration.*—Honorary Lieutenant-Colonel P. Hayes, T.D., R.A.M.C., retired.

*Two Clasps to the Territorial Efficiency Decoration.*—Colonel C. H. Budd, M.C., T.D., R.A.M.C., retired (honorary colonel of a Supplementary Reserve Unit); Lieutenant-Colonel T. H. Wilson, O.B.E., T.D., Major H. B. Trumper, T.D., and Captain J. D. A. Gray, T.D., R.A.M.C.

*First Clasp to the Territorial Efficiency Decoration.*—Major (Honorary Lieutenant-Colonel) E. M. R. Frazer, T.D., R.A.M.C.

*Territorial Efficiency Decoration and First Clasp.*—Major A. Chambers, R.A.M.C.

*Territorial Efficiency Decoration.*—Major (Honorary Lieutenant-Colonel) J. A. W. Segerdal and Captain (Honorary Major) P. D. C. Kinmont, M.B.E., R.A.M.C.

# Universities and Colleges

## UNIVERSITY OF CAMBRIDGE

Professor E. B. Verney, F.R.S., has been appointed representative of the University on the council of the Lister Institute of Preventive Medicine.

Dr. Dorothy H. Heard has been elected to the Gwynaeth Pretty studentship for three years from October 1.

In Congregation on June 20 the following medical degrees were conferred:

M.D.—R. G. Benians, J. A. Black, J. B. Foote, D. I. Williams, H. R. Jolly, J. R. May.

M.B., B.CHIR.—*By proxy:* W. Rodger.

## UNIVERSITY OF GLASGOW

The following degrees were conferred on July 7:

M.D.—J. Black, O. A. Finn, W. R. D. Hamilton (with commendation), D. Macaulay (with high commendation).

M.B., CH.B.—J. F. Adams, R. I. Alexander, V. G. Allan, A. W. Bain, G. Bain, W. M. Baird, G. Barr, Mary M. Baxter, J. M. Bell, Hazel M Boyd, Jean D. Brodie, Dorothy L. N. Brown, D. P. Brunton, J. McK. Buchanan, Marjory M. Buchanan, Grace A. Caddies, A. B. Cameron, K. A. Cameron, A. M. Campbell, Elizabeth M. Campbell, J. S. Campbell, P. Campbell, J. J. Casey, A. J. Childs, C. A. Clark, I. G. Conn, Margaret H. M. Craig, R. Craig, H. A. Crawford, J. Crooks, H. C. Cross, Lorna C. Cullen, Mary C. Cumming, Anne E. Currie, J. N. Cutler, C. M. Davidson, J. W. Dewar, R. E. Dickie, J. Dickson, Rosalie E. B. Eastwood, R. Emslie, A. Esterton, G. M. Ferguson, Isabella C. Ferguson, W. I. Forbes, Lois B. Ford, Joan M. Foyer, J. Frame, G. Fraser, Margaret Fyfe, W. Gardner, J. A. M. Garrett, I. Gavin, D. M. Gebbie, Jean A. Gemmell, E. O. Gibson, J. A. Gibson, D. A. MacK. Gillies, D. J. Godfrey, R. B. Goudie, J. R. Grant, W. Grindlay, Elizabeth G. Haggarty, G. Harris, J. L. Hastings, F. G. Hattersley, R. G. Haughie, V. M. Hawthorne, Dorothy W. S. Heiton, Isabella F. Henderson, C. H. Hodge, Elizabeth M. Hutton, Rosemary M. W. Ince, Katherine I. Jack, A. Jackson, U. Jacobson, J. W. Johnston, A. A. Johnstone, Margaret H. Kidd, A. G. King, J. C. Kirk, I. C. Lamont, R. MacG. Langmuir, A. Law, R. B. Lewis, A. Litton, Nancy J. Logan, D. B. McArthur, J. McArthur, A. S. MacAskill, A. W. McBryde, R. R. Macdonald, Christina C. McEwan, Agnes F. H. McFadyen, N. M. McFadyen, J. B. McGuinness, D. J. Mackay, D. E. Mackay, D. C. MacKeachan, L. D. Mackenzie, A. Mackinnon, J. McLaughlin, W. J. McLaughlin, M. L. McMillan, Ruby McMillan, Annie B. McNaught, P. H. McNellis, Morag W. McNicol, H. J. B. Manderson, Mrs. Jean McK. McEwen (née Mann), G. C. Mansfield, J. G. Marshall, M. B. Marshall, P. L. Martin, A. C. N. Millar, Margaret J. W. Miller, W. P. Mitchell, J. P. B. Morgan, T. C. Morton, J. B. J. Mulvey, W. R. Murdoch, D. M. Norwell, H. C. C. Nwankwo, C. O. Oshodi, I. W. Pinkerton, D. A. A. Primrose, D. C. Provan, A. Quinn, T. O. Ramsay, A. B. Reed, R. J. T. Reid, R. R. Renfrew, A. Reyburn, R. Richmond, J. L. Robertson, G. C. Robin, Jean M. N. Robotham, P. D. L. Roper, D. Ross, P. Ross, R. B. S. Ross, Mary McL. Sayers, B. J. Sherry, E. Sheville, L. F. Skinnider, R. S. Sloan, J. Smith, Mary E. C. Smith, C. P. Stewart, J. S. S. Stewart, D. C. Symington, H. F. Taggart, W. Taylor, J. D. Terrell, T. S. R. Train, D. Troup, P. I. T. Walker, W. M. M. Wallace, Catherine M. White, Gertrude H. M. White, Helen M. White, J. Willocks, J. L. Wilson, Sheila McC. Wilson, Winifred A. Wilson, B. Wolfson, E. W. F. Wood.

## UNIVERSITY OF DUBLIN

### SCHOOL OF PHYSIC, TRINITY COLLEGE

The following candidates have been approved at the examinations indicated:

M.D.—E. D. Kerr, J. B. C. Nabney, R. M. Pritchard.

M.A.O.—A. D. H. Browne.

FINAL MEDICAL EXAMINATIONS.—*Section (C), Medicine, and Section (D), Surgery:* [2]Doreen E. Mallagh, [2]J. G. Goodbody, [1 2]Patricia M. Leeson, [2]J. O. Farinde, [2]Patricia R. Hunter, E. Taylor, Ruth M. Ransom, H. G. Smith, Sheila E. Weir, Frances J. Baker, [3]W. Jackson, J. A. K. Meldrum, S. D. Coleman, Marian F. Cianchi, Margaret M. Bell, Prudence E. Park, T. Asuni, A. S. Dewar, Matilda M. Dickey, Patricia M. Woolf, Mary D. Brosnan, [3]Elizabeth M. Senior, Ethel P. Cole, J. R. Cole, S. P. Fitz-Simon Cotton, Hazel Morris, R. D. Thornes, J. R. MacN. Houston, [1]R. J. Weir, E. Ward, G. T. Nelson, W. Gault, Ethel A. L. Blake, J. Morrow, L. M. Dillon, Joan M. Falkiner, Norma E. Boyd, Audrey M. M. Fair. *Section (C), Medicine:* [2]H. M. O. Brown, R. King, B. W. Withrington, I. A. Eppel, Phyllis E. McCready, G. J. Malseed, E. D. Cooke, N. Boland, Edith P. Pringle, Ethel G. Jennings, W. A. Beatty, R. F. Hutchings, K. W. M. Harbord, T. E. W. Winckworth, J. Hunter, E. A. Otchere, A. W. L. Pollock. *Section (D), Surgery:* R. S. W. McLarnon, B. P. P. Judge, Daphne A. F. Laughlin, Patricia G. Ellis, J. P. Nixon, Aileen F. Smith, S. S. Faloon.

[1]With first-class honours in surgery. [2]With second-class honours in medicine. [3]With second-class honours in surgery.

The following medical degrees were conferred on July 5:

M.D.—E. D. Kerr, R. M. Pritchard.

M.B., B.CH., B.A.O.—T. Asuni, Frances J. Baker, Margaret M. Bell, Ethel A. L. Blake, Mary D. Brosnan, Marian F. Cianchi, Ethel P. Cole, J. R. Cole, S. D. Coleman, S. P. Fitz-Simon Cotton, A. S. Dewar, Matilda M. Dickey, L. M. Dillon, Audrey M. M. Fair, Joan M. Falkiner, J. O. Farinde, W. Gault, J. G. Goodbody, J. R. MacN. Houston, Patricia R. Hunter, B. P. P. Judge, Daphne A. F. Laughlin, Patricia M. Leeson, R. S. W. McLarnon, Doreen E. Mallagh, J. A. K. Meldrum, Hazel Morris, J. Morrow, G. T. Nelson, J. P. Nixon, Prudence E. Park, A. W. L. Pollock, Ruth M. Ransom, Elizabeth M. Senior, H. G. Smith, E. Taylor, R. D. Thornes, E. Ward, R. J. Weir, Sheila E. Weir, Patricia M. Woolf.

## QUEEN'S UNIVERSITY, BELFAST

At a graduation ceremonial on July 11 the honorary degree of M.D. was conferred on Mr. James Andrew Craig, consulting ophthalmic surgeon to the Royal Victoria Hospital, Belfast, and formerly lecturer in ophthalmology and otology in the University.

## UNIVERSITY OF MALAYA

On July 14 the degree of M.A. (*honoris causa*) was conferred on Dr. Charles A. H. Franklyn, Bedell of Convocation of the University of London, for services rendered to the University of Malaya. Dr. Franklyn is the first Englishman to receive the degree, which was conferred by diploma *in absentia*.

## ROYAL COLLEGE OF SURGEONS OF ENGLAND

The Royal College of Surgeons of England has been promised a licence for the first phase of its rebuilding, and work will start early in 1952. The biggest single item in its first phase will be the great hall, which is designed to seat 650 and to accommodate the largest and most important of the lectures, and will also be used for medical and surgical congresses, national or international. This hall will relieve a great need, as the College is at present much hampered by shortage of lecture-rooms. Over the great hall there will be three floors of museums, the gift of the Wellcome Trustees, which will provide a replacement of the museum rooms destroyed by enemy action. Also included in the first phase of building will be a new council room, an exhibition hall, and cloakrooms.

The principal feature of the remainder of the programme will be the Nuffield College of Surgical Sciences, and there will also be three additional floors of laboratories, extra lecture-rooms, and extensions of the library.

### FACULTY OF ANAESTHETISTS

At a meeting of the Board of the Faculty of Anaesthetists, held on June 23, Mr. A. D. Marston and Dr. Frankis T. Evans were re-elected Dean and Vice-Dean, respectively, of the Faculty for the ensuing year.

## ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following candidates were duly admitted licentiates in medicine and midwifery on July 7, having passed the final examination in medicine, surgery, and midwifery of the Conjoint Board of Ireland: T. M. Adair, A. G. Aitchison, Mary P. Bellew, T. F. Breen, T. J. F. Campbell, E. F. Cassidy, Marian E. Cox, E. O. A. Denloye, G. P. Dodd, A. T. E. Feanny, R. Feanny, B. G. Fleming, L. S. Galazka, J. M. Gray, Esther M. Heelan, W. O. Heffernan, Denise Hull, P. D. Lawler, K. Leddy, B. Lord, Z. J. Ludwig, H. J. Mathews, B. J. J. Murphy, P. T. McDonagh, D. C. McDonnell, G. V. McSwiggan, Miora G. O'Carroll, J. B. O'Sullivan, P. P. Rowan, J. A. Ryan, I. Smith, J. H. Taaffe, J. C. Williams.

## FACULTY OF RADIOLOGISTS

The following candidates have satisfied the Fellowship Board at the examination for the Fellowship held in May: F. M. Hooper (Radiodiagnosis), Margaret D. Snelling (Radiotherapy).

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending June 30 (No. 26).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

| Disease | 1951 Week Ending June 30 | | | | | 1950 Corresponding Week | | | | | 1942–50 England & Wales Corresponding Week | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | Highest | Median | Lowest |
| Diphtheria | 32 | 2 | 7 | — | — | 46 | 2 | 13 | — | 1 | 723 | 313 | 46 |
| Deaths | — | — | — | — | — | 2 | — | — | — | — | | | |
| Dysentery | 490 | 100 | 95 | 1 | | 262 | 9 | 113 | — | — | 292 | 123 | 49 |
| Deaths | | — | | — | | | | | — | | | | |
| Encephalitis, acute | 2 | — | — | — | | 5 | — | — | — | | 6 | 2 | — |
| Deaths | | — | | | — | | 1 | | | — | | | |
| Erysipelas | | | 10 | 2 | 5 | | | 33 | 4 | 1 | | | |
| Food-poisoning | 157 | 41 | | 4 | | 316 | 24 | | 5 | | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 9 | 25 | | | | | 31 | | | |
| Deaths | 5 | | 5 | 1 | — | 17 | | 4 | 2 | 2 | | | |
| Measles* | 10,060 | 230 | 246 | 200 | 179 | 8,918 | 626 | 405 | 106 | 291 | 9,377 | 6,984 | 2,503 |
| Deaths | | — | — | — | — | | — | — | — | 2 | | | |
| Meningococcal infection | 31 | 4 | 15 | 1 | 1 | 30 | 1 | 15 | 4 | 1 | 99 | 44 | 23 |
| Deaths | | — | — | | | | — | — | | | | | |
| Ophthalmia neonatorum | 42 | 3 | 10 | — | | 29 | 1 | 14 | — | — | 109 | 64 | 29 |
| Pneumonia, influenzal | 355 | 14 | 2 | 11 | 2 | 335 | 12 | 4 | 6 | — | 734 | 424 | 335 |
| Deaths (from influenza)† | 3 | 1 | — | — | — | 4 | — | — | 1 | — | | | |
| Pneumonia, primary | | | 144 | | | | | 159 | | | | | |
| Deaths | 126 | 20 | | 4 | 5 | 108 | 17 | | 8 | 5 | | | |
| Poliomyelitis, acute: | | | | | | | | | | | | | |
| Paralytic | 41 | 3 | 9 | 2 | 1 | 160 | 13 | 47 | 10 | 4 | 160 | 9 | 4 |
| Non-paralytic | 46 | — | | | | | | | | | | | |
| Deaths§ | — | — | | | — | 11 | 1 | | | — | | | |
| Puerperal fever | | | 8 | | | | — | 7 | | | | | |
| Puerperal pyrexia‖ | 53 | 8 | 4 | 5 | 1 | 70 | 10 | 7 | — | — | 161 | 125 | 70 |
| Scarlet fever | 904 | 72 | 133 | 22 | 42 | 1,085 | 63 | 131 | 57 | 67 | 1,982 | 1,255 | 947 |
| Deaths | | — | — | — | — | | | — | — | — | | | |
| Smallpox | — | — | — | — | | — | — | — | — | | | | |
| Deaths | | | | — | | | | | — | | | | |
| (1) Tuberculosis, respiratory | | | 144 | 36 | | | | 151 | 23 | | | | |
| (2) Tuberculosis, non-respiratory | | | 27 | 13 | | | | 21 | 9 | | | | |
| (1) Deaths | 123 | 15 | 12 | 4 | 7 | 162 | 19 | 23 | 3 | 12 | | | |
| (2) Deaths | | 3 | 3 | — | 4 | | 5 | 3 | 1 | 6 | | | |
| Typhoid fever | 1 | — | — | 3 | 3 | 7 | — | 1 | 1 | 2 | | | |
| Deaths¶ | — | — | — | — | | — | — | — | — | | 24 | 16 | 12 |
| Paratyphoid fever | 42 | 1 | 2 (B) | — | | 17 | 3 | — | — | 2 (B) | | | |
| Whooping-cough | 3,533 | 186 | 300 | 57 | 45 | 3,920 | 234 | 287 | 41 | 95 | 3,920 | 2,260 | 1,194 |
| Deaths | 4 | — | — | — | 2 | 5 | — | — | — | — | | | |
| Deaths (0–1 year) | 198 | 23 | 29 | 12 | 24 | 215 | 27 | 38 | 14 | 25 | 385 | 284 | 215 |
| Deaths (excluding stillbirths) | 4,110 | 633 | 533 | 101 | 156 | 4,081 | 636 | 491 | 110 | 159 | 4,660 | 3,982 | 3,726 |
| Annual death rate (per 1,000 persons living) | | | 10·8 | | | | | 9·9 | | | | | |
| Live births | 7,078 | 1,218 | 877 | 230 | 353 | 7,050 | 1,151 | 885 | 249 | 422 | 9,012 | 7,248 | 6,097 |
| Annual rate per 1,000 persons living | | | 17·7 | | | | | 17·8 | | | | | |
| Stillbirths | 173 | 27 | 24 | | | 186 | 19 | 22 | | | 276 | 194 | 181 |
| Rate per 1,000 total births (including stillborn) | | | 27 | | | | | 24 | | | | | |

* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

# Vital Statistics

## The Census

According to the preliminary report of the Registrar-General for England and Wales the population of England and Wales on April 8 this year was 43,744,924 persons, an increase of 9.5% over the population in 1931. These comprise 21,024,187 males and 22,720,737 females. The census was also carried out on that day throughout the rest of the British Isles and the Irish Republic. Some comparative figures given by the Registrar-General are shown in the table below, and the percentage increase or decrease over the 100 years is added in the last column.

| | Population in 1851 | Population in 1951 (*a*) | % Increase or Decrease |
|---|---|---|---|
| England (excluding Monmouthshire) .. .. | 16,764,554 | 41,147,938 | +145 |
| Wales and Monmouthshire .. | 1,163,055 | 2,596,986 | +123 |
| Scotland .. .. | 2,888,742 | 5,095,969 | +76 |
| Northern Ireland .. .. | 1,442,517 | 1,369,579 | −5 |
| Isle of Man .. .. .. | 52,387 | 55,213 | +5 |
| Jersey .. .. .. .. | 57,020 | 57,296 | +0·5 |
| Guernsey and associated islands .. .. .. | 33,719 | 45,474 | +35 |
| Irish Republic .. .. | 5,111,557(*b*) | 2,958,878 | −42 |

(*a*) All figures given in this column are provisional.
(*b*) The Military and Navy are not included in these figures.

Discussing regional increases since 1931 the Registrar-General points out that Birmingham's increase was 10.9%; its population is now over 1.1 million. Liverpool comes next with a population of about 750,000, and then Manchester with about 700,000. Sheffield and Leeds each have a population of about 500,000. The population of London Administrative County has decreased by 23.8% since 1931 from 4.4 million to 3.3 million.

Of the areas whose population has greatly increased since 1931, Huyton-with-Roby heads the list with an increase of 973%; Solihull and Gosport have also greatly increased, all being adjacent to large over-populated cities. Of the 27 areas with increases in excess of 50%, no fewer than 22 are within Greater London or within easy travelling distance of it. Though their growth was high after the outbreak of war, in general the rates of increase were far higher before 1939. The war and its aftermath of shortages and restraints must therefore have slowed the momentum of the earlier growth.

In England and Wales there are 1,081 females per thousand males, as compared with 1,096 in 1921 (an effect of the first world war) and 1,088 in 1931. The present ratio is remarkably higher than those of all earlier censuses up to 1911 and is indicative of the ageing of the population, for female mortality is much lower at the older ages.

A leading article on the census appears at page 163.

## Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in May was 204, compared with 125 (revised figure) in the previous month and 102 (revised figure) in May, 1950 (*Ministry of Labour Gazette*, June, 1951). Of these, 112 were deaths underground in coal mines. There were also 16 deaths of seamen —6 on trading vessels and 10 on fishing vessels.

There were 5 cases of lead-poisoning, 5 of anthrax, 14 of epitheliomatous ulceration, and 10 of chrome ulceration.

## Mumps and Diabetes

Under this heading Dr. W. P. D. Logan, Chief Medical Statistician at the General Register Office, discusses the results of an inquiry to test the hypothesis that mumps may be a cause of diabetes mellitus (*Monthly Bulletin of the Ministry of Health*, June, 1951). The inquiry showed no evidence of association between diabetes among adults and a history of mumps. Between August, 1949, and July, 1950, 43,041 persons aged 16 and over were asked by the Survey of Sickness carried out by the Social Survey whether they had ever had mumps. The answers were then tabulated according to whether or not the subject reported that he had been suffering from diabetes during the previous two months. The following table shows the percentage of persons interviewed who said they had definitely had mumps:

| | Persons With Diabetes | Persons Without Diabetes |
|---|---|---|
| Males, 16–64 .. .. .. | 21 | 25 |
| ,, 65 and over .. .. | 8 | 12 |
| Females, 16–64 .. .. .. | 35 | 35 |
| ,, 65 and over .. .. | 26 | 21 |
| Persons, 16 and over .. .. | 26 | 29 |

## Motor-cycle Fatalities

The report of the Registrar-General for 1949 shows that deaths of motor-cyclists still form an important proportion of the deaths of young men. In 1949 214 male motor-cycle riders aged 20–24 were killed. This number is two-thirds of the deaths resulting from motor-vehicle accidents at this age and is one-tenth of the deaths from all causes. At ages 25–34 the deaths of male motor-cyclists numbered 184, being one-half of the deaths from motor-vehicle accidents and one-fifteenth of the deaths from all causes. At all ages the deaths of male motor-cyclists, 700, formed one-quarter of the deaths from all motor-vehicle accidents.

W. J. Martin (*J. Hyg.*, 1935, **35**, 375) showed that the large death rate from road accidents among young adult males was responsible for the inflexion of the life table mortality which first appeared in 1930–2. The motor-cycle as a lethal machine is more deadly to its rider than to other road users. In 1949 700 male and 57 female motor-cycle riders were killed, while 18 pedal cyclists and 148 pedestrians died as a result of collision with a motor-cycle.

## Health in Stepney

In 1950 the infant mortality rate in Stepney was 26.55, the lowest recorded in the history of the borough and below the figure for England and Wales (29.8). In his annual report for the year Dr. F. R. O'Shiel, Medical Officer of Health, draws some comparisons between 1901 and 1950. In 1901 the average number of persons per house was 9.4, while in 1950 it was 3.5. The infant mortality rate in 1901 was 165 per thousand live births. Of the 283 samples of milk taken in 1901, 22% were adulterated, but in 1950 none of the 186 were.

## Quarterly Return for Scotland

The birth rate during the first quarter of this year was 18.8 per 1,000 and was 1.1 below the average of the five previous March quarters. The infant mortality rate was 46 per 1,000 registered live births. This rate was the same as that for the corresponding quarter of 1950 and was 10 below the five-year average. The general death rate was 17.8 per 1,000, being 2.8 more than the five-year average; it was the highest death rate for any quarter since the first quarter of 1941.

The death rate from respiratory tuberculosis was 51 per 100,000 and that from other forms of tuberculosis was 7; the former rate was 7 below and the latter rate the same as the rate for the first quarter of 1950. The rates were 15 and 5, respectively, below the average of the first quarters of 1946–50. 984 deaths during the quarter were attributed to the principal infectious diseases. They included 899 from influenza, 52 from whooping-cough, and 23 from cerebro-spinal fever.

### Poliomyelitis

Poliomyelitis notifications in the week ending July 7 were as follows (figures for the previous week are in parentheses): paralytic 40 (41), non-paralytic 60 (46); total 100 (87). Up to and including the week ending July 7 the overall notification rate for England and Wales was 2.06 per 100,000, with the highest rates in the midland and south-western regions—3.89 and 2.99 respectively—and the lowest in the north-western and northern regions—1.44 and 1.50 respectively.

Of particular interest in the current year is the marked tendency towards a high proportion of non-paralytic cases. This is demonstrated by the following figures:

| | | | |
|---|---|---|---|
| 1950 | corrected notifications—Non-paralytic cases | | =28% |
| 1951 | uncorrected notifications: | | |
| | 1st–27th week | Non-paralytic cases | =37% |
| | 24th–27th " | " " " | =53% |
| | 27th " | " " " | =60% |

This tendency has been particularly great in the more recent weeks. The reason is at present difficult to assess. But it is clear that the numbers of paralytic cases until now are materially fewer than the total notifications would under normal circumstances indicate.

As regards individual districts in England and Wales in the period to July 7, 25.4% had reported one or more cases since the beginning of the year. Some of those with the largest numbers of notifications in this period were as follows (rate per 100,000 in parentheses): Coventry C.B. 67 (26.13), Orpington U.D. 22 (37.18), Rotherham R.D. 10 (21.30), Flint M.B. 7 (49.42), St. Austell R.D. 6 (38.16).

### Infectious Diseases

The number of notifications of infectious diseases in England and Wales during the week ending June 30 decreased for measles 1,263 and dysentery 77, and increased for whooping-cough 97 and scarlet fever 47.

The largest falls in the number of notifications of measles were Devon 190, Lancashire 133, Durham 125, Cheshire 121, Cumberland 111, Essex 109, and London 105; notable exceptions to the decreasing incidence were rises in Buckinghamshire 103 and Warwickshire 57. No alteration of any size occurred in the local returns of scarlet fever. The notifications of diphtheria were 5 fewer than in the preceding week; the largest variations in the local trends were a decrease of 4 in Durham and Yorkshire West Riding. The largest rises in the number of notifications of whooping-cough were Lancashire 71 and Kent 42, and the largest fall was Devon 40.

Of the 42 cases of paratyphoid fever, 19 were notified in Lancashire. These cases were scattered over nine administration areas.

The notifications of acute poliomyelitis were 8 more than in the previous week. The largest centres of infection were Warwickshire 22 (Birmingham C.B. 7, Coventry C.B. 12), Yorkshire West Riding 17 (Leeds C.B. 4, Rotherham R.D. 4; the remaining 9 cases involved 7 administration areas), Middlesex 5, and Derbyshire 5.

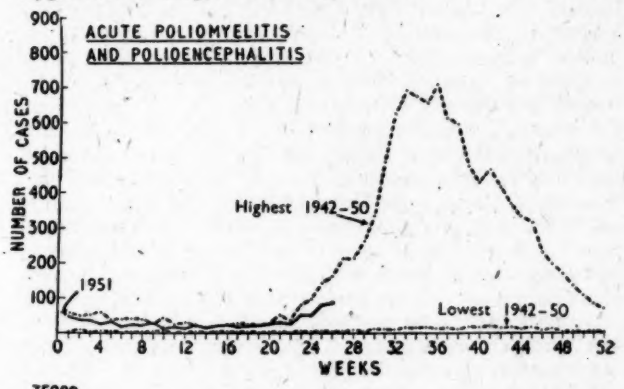
For the first time for 32 weeks the notifications of dysentery were below 500. The chief feature of the returns was a fall of 51 in Kent. The largest returns were London 100 (these cases were scattered through 24 boroughs), Middlesex 79 (Edmonton M.B. 26), Yorkshire West Riding 56 (Brighouse M.B. 23, Sheffield C.B. 17), Lancashire 48, Kent 34 (Malling R.D. 26).

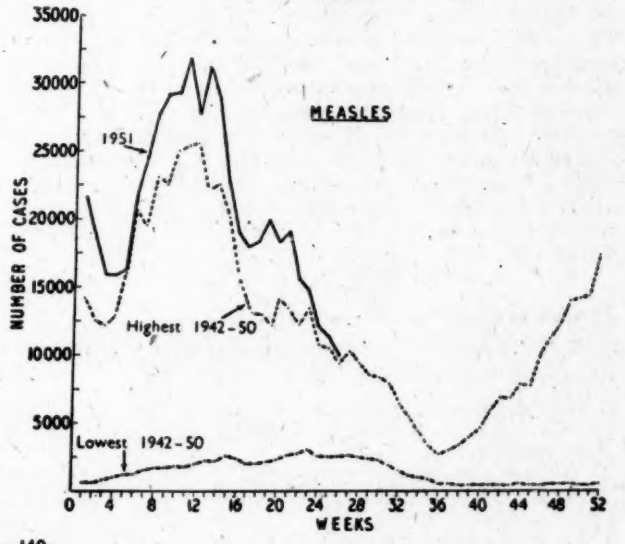
### Week Ending July 7

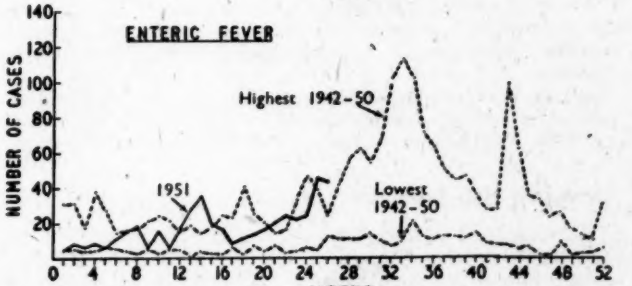
The notifications of infectious diseases in England and Wales during the week included: scarlet fever 816, whooping-cough 3,358, diphtheria 22, measles 8,544, acute pneumonia 358, acute poliomyelitis 100, dysentery 368, paratyphoid fever 23, typhoid fever 7.

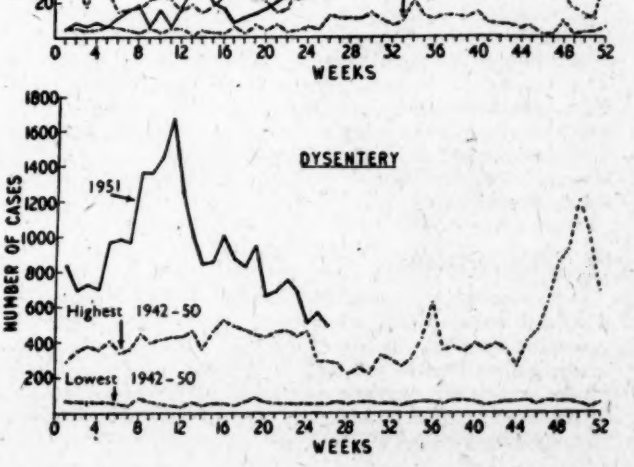
### Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus -------, the figures for 1951 thus ————. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.



# Medical News

### Opening of International Congress of Clinical Pathology

The first International Congress of Clinical Pathology was opened in London on Monday, July 16, by the Minister of Health. Dr. S. C. Dyke, President of the International Society, in welcoming pathologists from about 20 countries, paid a special tribute to the French Society of Clinical Biology, which sponsored the International Congress in that subject in Paris in 1947, on which occasion the International Society of Clinical Pathology was founded. He looked forward to a network of national societies throughout the world, providing for an exchange not only of information and ideas but also of pathologists. He then invited Sir Lionel Whitby, as President of the Association of Clinical Pathologists, to take the chair. The Minister of Health said that this country had sought, through its National Health Service, to make available modern developments in clinical pathology to all its citizens according to their need. A vote of thanks to the Minister was proposed by Professor Robert Cruickshank, chairman of the Executive Committee, and was seconded in Italian by Dr. T. de Sanctis Monaldi. Sir Lionel Whitby then delivered an address on "Science and Art in Medicine." He had chosen this title, he said, because he believed that clinical pathology came nearer to combining these two approaches to medicine than did any other specialty. Professor M. Polonovski proposed the vote of thanks, seconded by Dr. A. Seelek. The congress began its real work, in four sections, devoted respectively to haematology, histopathology, chemical pathology, and microbiology, on Tuesday morning, and continued until Friday, July 20.

### Dangerous Drugs Act

The following have been added to Part III of the Schedule, which controls trading in drugs:

Dihydrocodeine, its salts and any preparation, admixture, extract, or other substance containing any proportion of dihydrocodeine.

Acetyldihydrocodeine, its salts and any preparation, admixture, extract, or other substance containing any proportion of acetyldihydrocodeine.

4-Propionoxy-4-phenyl-1-methyl-3-ethylpiperidine, its salts and any preparation, admixture, extract, or other substance containing any proportion of 4-propionoxy-4-phenyl-1-methyl-3-ethylpiperidine.

3-Hydroxy-N-methylmorphinan, its salts and any preparation, admixture, extract, or other substance containing any proportion of 3-hydroxy-N-methylmorphinan: now known as methorphinan.

### Sir Arthur Hall Memorial Lecture

The Sheffield Medico-Chirurgical Society has decided to commemorate the memory of the late Sir Arthur Hall by establishing a memorial lecture to be delivered triennially on a subject of medical interest. The society hopes that many Sheffield medical graduates not necessarily connected with the society will wish to subscribe to the endowment fund for the lecture, and donations should be sent to the honorary treasurer, Mr. E. Gordon Mackie, 287, Glossop Road, Sheffield, 10.

### First Woman Dentist

Dr. Lilian Lindsay qualified in 1895, the first woman in Britain to become a dental surgeon. On July 4 last she was presented with her portrait during the 71st annual meeting of the British Dental Association; in 1946 she was president of the association, and she still works as honorary librarian at the headquarters in Mayfair. Dr. Lindsay will celebrate her eightieth birthday on July 24.

### Princess Elizabeth, F.R.C.O.G.

At a simple yet dignified ceremony on July 17 Princess Elizabeth was admitted to the Honorary Fellowship of the Royal College of Obstetricians and Gynaecologists. The two sponsors for the new Fellow, Sir William Gilliatt and Professor R. W. Johnstone, Senior Fellow in Scotland, paid brief and graceful tributes to one who was "an inspiring model to young womanhood," Professor Johnstone concentrating particularly on the special attributes of the Duchess of Edinburgh. The President of the College, Dame Hilda Lloyd, after admitting Princess Elizabeth to the Fellowship, spoke of the great satisfaction it gave to the College to be able to confer the highest honour in their power on Princess Elizabeth two years after the Queen had accepted the same honour. The new Fellow, in a brief reply, congratulated the College on the great work it was doing for mothers and babies, not only in the Commonwealth but all over the world.

## COMING EVENTS

### Industrial Radiology Summer Meeting

The Industrial Radiology Group of the Institute of Physics will hold a meeting and exhibition at 47, Belgrave Square, London, S.W.1, July 23 to 25. On the first day Mr. D. Bromley will give an analysis of the quality of radiographs, and Mr. J. Rhodes will talk on gamma-ray stereography. Other topics include xeroradiography and short-range radiography (July 25). Application should be made to the deputy secretary, Institute of Physics, 47, Belgrave Square, London, S.W.1, not later than July 18.

### Oto-rhino-laryngology Congress

The second French congress will be held at the Faculty of Medicine, Paris, October 22 to 25 inclusive. The subjects will be the surgical treatment of bilateral adduction paralysis of the larynx and naso-sinus allergy. Full information may be obtained from the general secretary, Dr. H. Flurin, 19, Avenue MacMahon, Paris, 17e.

## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

**Saturday**

RENAL ASSOCIATION.—At Ciba Foundation, 41, Portland Place, London, W., July 21, 11 a.m., *"Renal Clearances in Disease,"* by Dr. S. E. Bradley.

**Monday**

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Edinburgh University (Anatomy Lecture Theatre), July 23, 4.30 p.m., *"Recent Advances in Biochemistry and Their Repercussion on Nutrition Problems,"* by Professor E. J. Bigwood.

●INSTITUTE OF CHILD HEALTH.—At Hospital for Sick Children, Great Ormond Street, London, W.C., July 23, 5 p.m., *"Retrolental Fibroplasia,"* Guest Lecture by Professor Marcel Lelong (Paris).

**Tuesday**

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—July 24, 2.30 p.m., *"Physical Treatment in Neurological Diseases,"* clinical demonstration in neurology by Dr. James W. Byrne.

**Wednesday**

●MINISTRY OF LABOUR AND NATIONAL SERVICE.—At Safety, Health, and Welfare Museum, Horseferry Road, Westminster, London, S.W., July 25, 3 p.m., *"The Effect of Environment on the Health and Efficiency of the Industrial Worker,"* by Professor R. E. Lane. (Tickets from Director of Public Relations of the Ministry, 8, St. James's Square, London, S.W.1.)

**Friday**

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES, 11, Chandos Street, Cavendish Square, London, W., July 27, 7.30 p.m., annual general meeting; *"Some Notes on the History of Congenital Syphilis,"* presidential address by Dr. Mary M. Shaw

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Ashford Hospital, July 27, 5 p.m., *"Privilege and Responsibility,"* John Tate Lecture by Sir Francis Fraser.

## APPOINTMENTS

MINISTRY OF EDUCATION.—*Principal Medical Officer*, Peter Henderson, M.D., D.P.H. (in succession to Dr. J. E. A. Underwood, who retired on June 30); *Senior Medical Officer*, A. F. Alford, M.B., Ch.B.

Dr. Henderson qualified at Aberdeen in 1929 and proceeded M.D. in 1931, taking the D.P.H. the next year. He was formerly medical officer of health for the borough of Todmorden before entering the Ministry of Education as Medical Officer.

Dr. Harry Sutherland Gear, deputy chief health officer in the Union of South Africa, has been appointed assistant director-general of the World Health Organization, in succession to Sir Sahib Singh Sokhey, who will retire on reaching the age limit next April.

Dr. Gear, who was born in 1903, received his medical education at the University of the Witwatersrand, graduated B.Sc., with first-class honours, in 1925, taking the M.B., B.Ch. three years later. He proceeded M.D. in 1938. In 1931, after studying at the London School of Hygiene and Tropical Medicine, he took the D.P.H. of the University of London and in the following year the D.T.M.&H. of the Royal Colleges. From 1932 to 1935 he was in charge of the Department of Preventive Medicine and Medical Statistics, Lester Institute, Shanghai, and from 1935 until the present time he has been on the staff of the Union Health Department in South Africa, except for the period 1940–4, when he served as a senior medical officer with the South African and British armed Forces in East Africa and the Eastern Mediterranean region.

---

DREW, DEIRDRE M., M.B., B.Ch., D.C.H., Junior Medical Officer, St. Mary's Chest Hospital, Phoenix Park, Dublin.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Part-time Assistant Ophthalmologist, West Suffolk Hospital and White Lodge Hospital*, Kathleen M. Long, F.R.C.S.Ed., D.O.M.S. *Surgical Registrar, Peterborough and District Memorial Hospital*, J. V. Coyle, M.B., Ch.B.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*Surgical Registrar (Senior Registrar Grade)*, J. F. R. Bentley, F.R.C.S. *Part-time Ophthalmic Registrar (Senior Registrar Grade)*, J. G. Madden, M.B., B.Ch., D.Ophth. *Junior Resident Anaesthetist (Senior House Officer Grade)*, Janet P. Rickard, M.B., B.S. *Assistant Resident Medical Officer, Tadworth (Senior House Officer Grade)*, Helenor F. Lochhead, M.B., Ch.B. *House-physicians (Senior House Officer Grade)*, B. E. R. Symonds, M.D., M.R.C.P., D.C.H., J. S. McKim, M.Sc., M.D. *House-surgeon (Senior House Officer Grade)*, J. M. Jones, M.B., B.S., F.R.C.S.Ed.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—*Full-time Obstetrician and Gynaecologist, Oldchurch Hospital*, J. D. Watt, M.B., Ch.B., M.R.C.O.G. *Part-time Obstetrician and Gynaecologist, Bethnal Green Hospital*, J. J. F. O'Sullivan, M.B., B.Ch., M.R.C.O.G. *Part-time General Physician, St. Clement's and St. Andrew's Hospitals*, J. A. Robertson, M.B., B.S., M.R.C.P.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Alms.**—On July 8, 1951, at the Bristol Maternity Hospital, to Beryl Elizabeth (formerly Norris), wife of Dr. Michael Alms, a daughter.

**Gresham.**—On July 7, 1951, at King's College Hospital, to Gwen (formerly Leigh), wife of Dr. G. Austin Gresham, a son.

**Hulbert.**—On July 5, 1951, to Elizabeth (formerly Brockman), wife of Mr. K. F. Hulbert, F.R.C.S., Woodlands, St. John's Road, Petts Wood, Kent, a son.

**Standeven.**—On July 8, 1951, to Patricia, wife of Alfred Standeven, F.R.C.S.Ed., of Pendle House, Tredcroft Road, Hove, a daughter.

### DEATHS

**Bathurst.**—On July 12, 1951, in London, Lulium Wood Bathurst, M.D., of 15, Inverness Terrace, London, W., aged 83.

**Burges.**—On July 8, 1951, at 26, Brecon Road, Handsworth, Birmingham, Frederick Augustus L'Estrange Burges, O.B.E., M.R.C.S., L.R.C.P., aged 81.

**Carding.**—On July 5, 1951, at 9, Bromley Grove, Shortlands, Kent, Mary Wilson Carding (formerly Batchelor), M.B., Ch.B.

**Cassels.**—On July 8, 1951, at Bristol, Thomas William Cassels, F.R.C.S.Ed., of 26, Queen's Court, Clifton, Bristol.

**Gellatly.**—On July 5, 1951, Robert Gellatly, M.B., C.M., of Dudd House, Meltham, Huddersfield, aged 77.

**Gooch.**—On July 2, 1951, at Ragleth House, Church Stretton, Salop, Horace Gooch, M.B., B.S.

**Gordon.**—On July 7, 1951, at the Victoria Hospital, Kirkcaldy, Edward Skene Gordon, M.B., Ch.B.

**Graham.**—On July 4, 1951, at Taunton, George Taylor Graham, M.B., Ch.B., of Inverkeithing, Fife, aged 28.

**Hearn.**—On July 13, 1951, at Torquay, Edward Michael William Hearn, O.B.E., M.R.C.S., L.R.C.P., Surgeon Commander, R.N., retired.

**Ludgater.**—On July 8, 1951, at Burton-on-Trent, Geoffrey Goulden Ludgater, M.B., B.Chir., of 23, Osborne Street, Winshill, Burton-on-Trent, aged 45.

**Mearns.**—On June 29, 1951, at the Brompton Hospital, London, S.W., George Walter Mearns, M.B., Ch.B., Government Medical Service, British Guiana.

**Stephen.**—On July 5, 1951, at the De la Pole Hospital, Willerby, Yorks, Mabel Stephen, M.B., Ch.B., aged 50.

**Taffs.**—On June 28, 1951, at King's College Hospital, Evelyn Nora Taffs, L.R.C.P.&S.I.&L.M., of 97, Denmark Hill, London, S.E., aged 60.

**Thompson.**—On July 13, 1951, at Canterbury, John Knox Stafford Thompson, M.B., F.R.C.S.Ed., of Treetops, Stodmarsh Road, Sturry, Kent, formerly of Clontibret, Co. Monaghan, Northern Ireland.

# Any Questions?

*Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.*

### Trichomonas Vaginalis

**Q.**—*How is infection by Trichomonas vaginalis transmitted? Can it be a venereal disease?*

**A.**—It has been established beyond reasonable doubt that *Trichomonas vaginalis* infection can be transmitted by coitus. This, however, accounts for only a small proportion of cases of trichomonas vaginitis, and the method of infection in the remainder is unknown.

A large number of women, sometimes estimated at 20 to 25%, are carriers of the organism, and it may be that in these any illness or circumstance which lowers local or general resistance is enough to precipitate an attack of vaginitis. Nevertheless there is a widespread belief among gynaecologists that women not infrequently contract the infection from one another, especially when they are living in a close community. Thus it is not uncommon for trichomonas vaginitis to occur in a woman who has recently been in hospital, and it is suggested, although not proved, that the infection is transferred from a carrier or another infected woman who happens to have been in the same ward, the mechanism of transfer being the ward baths. If this idea is correct, then hotel baths are another possible source of danger.

### Fainting at the Sight of Blood

**Q.**—*A man, aged 30, complains bitterly of being subject to fainting at the sight of blood, and he "feels queer" even at the mention of bleeding. Any sort of idea of bodily injury makes him feel uncomfortable (either injury to himself or others). He is physically perfectly sound and extremely active. In all other respects he seems to be psychologically normal. This trouble was with him from his earliest days until about the age of 20, when he became quite free from this disability, but it has recently returned. It is now so bad as to make everyday life difficult. Is there anything that can be done for him?*

**A.**—A man of 30 who from childhood to the age of 20 so feared the sight or thought of blood that he fainted or "felt queer" has most likely a hysterical problem. In other words he has probably forgotten some early anxious association of blood and childish ideas of sexuality, and only remembers the association of faintness and blood. Poorly understood experiences of childbirth or menstruation are often the basis of such troubles. Such hysterical symptoms often disappear when the patient makes some kind of adjustment to his adolescent sexuality, only to reappear when life faces him with new problems. Less commonly, such phobias are part of an obsessional neurosis.

The type of treatment needed will depend upon the severity of the problem. The simplest treatment is based on a detailed history. When the changing symptoms of the neurosis and the crucial events of sexual development and personal life are listed and dated, the coincidence in time between a change in symptoms and some specially significant event in life will often become apparent. If such a coincidence and the likelihood of his having forgotten some important emotional experience or attitude is then pointed out to the patient, and if he is reassured that now as an adult he will be able to cope with emotional problems which he could not face squarely as a child, and if he is asked to talk about himself, he may be surprised to find how much understanding he can develop. One can reassure him that by learning to talk about his difficulties he is proving to himself

that he can think and feel in a healthy manner. The patient described in the question could also be encouraged by pointing out to him that, since he rid himself of his troubles for 10 years without developing any insight into their cause, he may now be able to dispense with them for good by coming to a better understanding of himself. He can be reassured at the beginning of the interview that if he does not improve by talking things out there is help available elsewhere, and he may well be led to work out his problem in this way.

Many simple phobias can be solved along the lines indicated, and it is only by trying minor psychotherapy and being willing to risk failure at first that the general practitioner will develop the skills which lead to success.

### Carpenters' Dermatitis

Q.—*Is dermatitis a known occupational risk of carpenters? I have a patient with an eczematous eruption of recent origin on both forearms. He has been working lately on thuja (arbor vitae), an unusual wood for him to handle. Could the thuja have been responsible for the eruption?*

A.—Dermatitis is a recognized occupational risk among carpenters: workers in wood appear to require compensation about one and a half times as frequently as those in other industrial occupations. The hands and forearms are the most commonly affected sites. Apart from non-specific factors such as friction, use of unsuitable cleansing agents, etc., the rashes in wood-workers may be caused by specific irritants or sensitizing substances such as glue, resins, or lacquers, as well as by wood itself. Arbor vitae (*Thuja* sp.) is known occasionally to induce eruptions, chiefly among gardeners (see Schwartz, Tulipan, and Peck; *Occupational Diseases of the Skin*, p. 583, 1947. Philadelphia).

### Facial Scars in Women

Q.—*What is the best way of concealing a burn scar on a woman's cheek? The scar is 20 years old, 4½ in (11.4 cm.) in diameter, and, apart from one or two areas of redness, appears healthy.*

A.—It should be possible to conceal this scar by the application of a cover cream (there are now several applications of this type on the market). Such treatment will be successful only if the scar is soft and flat. Irregularity of the scar or instability of its surface, or contraction with distortion of the surrounding parts, would call for excision of the scar and skin replacement.

### Auriculo-temporal Syndrome

Q.—*What is the auriculo-temporal syndrome? How is it caused and what is the treatment?*

A.—The auriculo-temporal syndrome is a rare sequel to parotid suppuration or injury and was first described by Frey in 1923 (*Rev. neurol.*, 1923, **2**, 97). Cases have been reported, especially from Eastern Europe and Russia, following parotitis secondary to typhus or typhoid fever, but the condition may follow any type of severe parotid infection. The syndrome, which may develop weeks or months after the original lesion, is characterized by hyperaemia and sweating in the distribution of the auriculo-temporal nerve, and these manifestations sometimes spread to the surrounding skin area. Sweating is sometimes so profuse that the patient has to wrap a towel round his head. The attacks frequently develop in response to gustatory stimuli: some patients notice that hot and spicy foods are especially liable to precipitate an attack, but the chewing of tasteless substances has no effect.

The exact cause of this condition is unknown. It has been suggested that it is due to taste stimuli from the posterior third of the tongue being diverted from the usual reflex channels as the result of abnormal communications between parotid secreting fibres and the sweat and vasomotor fibres in the auriculo-temporal nerve. According to this hypothesis there is faulty regeneration of the damaged secretory fibres. This ingenious explanation does not, however, account for the flushing of the face.

Treatment is difficult. Avulsion of the auriculo-temporal nerve, or its injection with alcohol, has been tried, but there is no reliable evidence about the value of this therapy; the symptoms are not relieved by atropine in ordinary doses. The condition is usually persistent, although there may be spontaneous improvement with the passage of time.

### Gas Fire at Eye Level

Q.—*A gas fire has been built into the wall of a sitting-room so much above the floor that the heat from the fire falls on the face of any person sitting in front of it. What is the risk of this ultimately injuring the eyes?*

A.—Regular exposure of the eyes for many years to infra-red radiation from very hot sources, such as molten glass or metal, may lead to "heat cataract." It is unlikely that any such injury would result from exposing the eyes to radiant heat from a gas fire, as the temperature is not nearly so high as with the industrial heat sources associated with the occurrence of cataract. Exposure of the face and head to the radiant heat from a gas fire does, however, result in discomfort—and this may be considerable—so that the positioning of a fire as described in the question is to be deprecated.

### Sensitivity to Local Sulphonamide

Q.—*Can sensitivity be caused by the local use of sulphonamides as nasal or eye-drops, or as ointments?*

A.—Yes. Sensitivity is on the whole rather more readily produced by superficial application, if this is continued for more than five days, than by systemic administration, and some authorities have discouraged such forms of use for that reason.

### Active Immunization after Severe Reaction to Antitetanus Serum

Q.—*I wish to immunize actively with tetanus toxoid a patient who has had a severe anaphylactic reaction to antitetanus serum. Is there any risk in doing this, and if so how can it be avoided?*

A.—The reaction to tetanus antitoxin in this case was presumably due to previous sensitization to horse protein, since antitoxic sera are mostly prepared in the horse. Tetanus toxoid, on the other hand, is prepared from nutrient broth, where any foreign protein is already broken down to peptones and amino-acids which do not act as sensitizing agents. It is therefore very unlikely that the patient will show any reaction to injections of tetanus toxoid. As a precaution, however, it would be wise to give a preliminary *intradermal* injection of 0.1 ml. of the toxoid. If there is no spreading weal or erythema it will be safe to continue with the two subcutaneous injections of 1.0 ml. toxoid at 6 weeks' interval.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 2111. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 2111. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.